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(54) Carbon-clad inorganic oxide particles with a polymer coating thereon.

(57) A carbon-clad inorganic oxide particle having an outermost cross-linked polymer coating. Carbon-clad inorganic oxide particles may be formed by placing a plurality of the particles in a reaction chamber, elevating the temperature within the chamber, reducing the pressure within the chamber, and introducing into the chamber a vapor comprising carbon and thermally decomposing the vapor so as to deposit a cladding of carbon onto the particles. The carbon-clad particles may be coated with a monomer or an oligomer followed by cross-linking the monomer or oligomer to provide polymer-coated carbon-clad inorganic oxide particles.

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Field of the Invention

The present invention provides carbon-clad inorganic oxide particles having a polymer coating thereon. The particles are useful as a chromatographic support material. The invention also provides a method for forming a chromatographic support material, by providing carbon-clad inorganic particles and then coating the same with a monomer or oligomer, and cross-linking the monomer or oligomer to form polymer-coated carbon-clad particles.

Summary of the Invention

The present invention provides a composite support material which is useful as a stationary phase in liquid chromatography, particularly in high-performance liquid chromatography. The composite support material comprises carbon-clad inorganic oxide particles which are coated with an outermost layer of an organic polymer. The particles can be coated by adsorbing a polymerizable monomer or oligomer onto the surface of the carbon-clad particles, and subsequently cross-linking the monomer or oligomer, e.g., by reaction with a free radical initiator or by irradiation. Useful inorganic oxides include, but are not limited to, the Group II, III and IV metals, i.e., HfO_2, ZrO_2, SiO_2, Al_2O_3, TiO_2 and MgO. solute retention during exposure to increasing amounts of alkaline mobile phase.

Preferred carbon-clad ZrO_2 spherules useful for liquid chromatography applications will comprise a porous core ZrO_2 spherule. The core spherules will preferably have a diameter of about 1-500 μ, more preferably about 2-50 μ; a surface area of about 5-300 m^2/g, more preferably about 15-100 m^2/g; and a pore diameter of about 20-5000 Å, more preferably about 60-1000 Å.

In addition to the core ZrO_2 spherule, the support material of the present invention further comprises a cladding of carbon. As used herein, the phrase "carbon-clad" means that an outer layer, sheath, coating, or cladding of pyrolytic carbon is bonded or otherwise integrally attached to the underlying ZrO_2 matrix. As used herein, "pyrolytic carbon" is intended to refer to carbon formed by the carbonization of a suitable carbon source, e.g., a hydrocarbon. "Carbonization" means that the hydrocarbon or other carbon source is subjected to conditions causing it to decompose into atomic carbon and other substances.

As mentioned above, the ZrO_2 cores of the carbon-clad particles are porous. When discussing porosity, the term "open pores" refers to interior channels in the particles which exit at the surface of the particle. The term "closed pores" refers to pores which have no exit at the outside surface of the particle. The surface of closed pores are inaccessible to either gas or liquid phases with which the particles are contacted. Thus, the closed pores are not affected by the cladding process, nor do they participate in subsequent use of the particles in surface active applications. As used herein, the term "pores" (or "porosity") refers to "open pores" only. By "surface of the particle", it is meant the exterior surface as well as the surface of the open pores. It is intended that the carbon cladding cover

In order to facilitate packing of liquid chromatography columns, it is preferred that each individual unit of the present support material be a substantially spherical particle; thus, the preferred spherical particles will be referred to herein as "spherules." However, the present invention is also intended to provide support materials useful in low performance chromatography, fluidized beds, and general batch absorbers. There is no requirement that the present particles be substantially spherical in these applications, where irregularly shaped particles are typically utilized.

Carbon-clad ZrO_2 particles display very high physical and chemical stability in aqueous media of high pH, e.g., pH 14. At these conditions, the particles are substantially resistant to dissolution of both the carbon cladding and the underlying ZrO_2, and provide substantially constant substantially all of the surface of the spherule, thus defined. As used herein, "substantially covering" or "substantially all" means that at least about 75%, preferably at least about 90%, and more preferably at least about 95% of the total surface area of the core ZrO_2 spherule will be covered by the carbon cladding.

Preferably, the thickness of the carbon cladding over the surface of the ZrO_2 core ranges from the diameter of a single carbon atom (a monatomic layer), to about 20 Å. This carbon cladding will thus not appreciably increase the diameter of the spherules. Thus, preferred carbon-clad ZrO_2 spherules will have a diameter of about 1 - 500 microns and more preferably about 2-50 μ. The carbon-clad ZrO_2 spherules will preferably have an average pore diameter of about 20 - 5000 Å, more preferably about 60-1000 Å. The carbon-clad ZrO_2 spherules will also preferably have a surface area of about 5 - 300 m^2/g, more preferably about 15-100 m^2/g.

Carbon-clad ZrO_2 particles which are essentially non-porous are also useful. Prior to carbon cladding, preferred non-porous ZrO_2 substrate particles will have a diameter of about 0.4-7 microns, a surface area of about 0.1-3 m^2/g, and negligible internal porosity, although the particles may have surface roughness.

Useful non-porous ZrO_2 having the preferred diameter and surface area values can be prepared by methods well known to those of ordinary skill in the art of ceramic powder preparation. The carbon-clad non-porous particles are believed to be particularly useful as a stationary phase support material in liquid chromatography separations of large molecules such as proteins and polymers. The size of such molecules can hinder or prohibit their rapid diffusion in and out of pores of a porous support material.

A method for forming a chromatographic support material utilizing chemical vapor deposition comprises the steps of:

(a) placing a plurality of porous inorganic oxide particles having a surface within a reaction chamber; (b) establishing an elevated temperature within the reaction chamber, e.g., of about 500-1500°C; (c) establishing a reduced pressure within the reaction chamber, e.g., of less than about 760 mm mercury; and (d) introducing a vapor comprising carbon into the chamber so as to decompose the vapor and deposit a cladding of the carbon onto the particles, substantially covering the surface of the particles. The method may also optionally include an additional step (e) of exposing the carbon-clad particles of step (d) to a gaseous reducing mixture comprising hydrogen so as to cause the reduction of polar functional groups on the surface of the particles. In this manner, a more homogeneous surface chemistry can be achieved.

The method is applicable to any inorganic oxide substrate to which carbon will deposit under the operating conditions of the method. Useful inorganic oxides include, but are not limited to the Group II, III, and IV metals, i.e., HfO_2, ZrO_2, SiO_2, Al_2O_3, TiO_2, and MgO. Preferably, a ZrO_2 or HfO_2 substrate is utilized in the method, because the core ZrO_2 or HfO_2 particles maintain a useful surface area at the high process temperatures (e.g., about 500-1500°C) which are preferred for forming uniform CVD coatings. In contrast, the porous network of alternative substrates, such as silica and alumina particles, may substantially degrade at these temperatures, with a resulting surface area loss which may compromise the chromatographic character of these substrates. Furthermore, ZrO_2 or HfO_2 are especially preferred substrates because their high chemical stability means that exposure of incompletely carbon-clad ZrO_2 or HfO_2 particles to aggressive mobile phases (e.g., pH 14), will not result in attack of the support with eventual dissolution. ZrO_2 is particularly preferred because it is much less expensive than HfO_2.

The above-described method for forming a chromatographic support material, utilizing chemical vapor deposition can also be used for forming an essentially non-porous support material, such as the non-porous carbon-clad ZrO_2 described above. When desired, step (a) of the method will comprise the step of placing a plurality of essentially non-porous inorganic oxide particles having a surface within a reaction chamber. The remaining steps (b) through (d) (and optionally step (e)) of the method are not changed by the utilization of a non-porous substrate.

Although the inorganic oxide particles have outer surfaces substantially covered with a carbon cladding as defined hereinabove, some inorganic oxide sites may remain exposed. These exposed sites may serve as sites for adsorption of oxygenated species such as carbonates, sulfates, phosphates, and carboxylates. Such adsorption may lead to inefficient chromatographic performance and poor peak shape. The carbon cladding of these particles may also exhibit strong interactions with certain species such as polar aromatic compounds, further decreasing chromatographic efficiency. Moreover, the presence of oxygenated sites on the carbon cladding can result in a surface which is energetically heterogenous, which in turn can cause a loss of chromatographic peak resolution.

The present invention addresses these problems by employing a further polymeric coating over the carbon-clad surface of the particles. Utilization of a non-polar polymeric coating renders the carbon-clad inorganic oxide particles substantially hydrophobic and provides a more energetically homogenous surface. The polymer coating can improve the spectrum of properties of the support, e.g., loading and efficiency, without significantly altering any of its desirable physical and mechanical properties.

In the majority of reversed-phase liquid chromatography applications, a hydrophobic stationary phase material is required. Thus, hydrophobic polymer-coated, carbon-clad particles according to the present invention are a useful support for reversed phase liquid chromatography. Alternatively, the carbon-clad particles can be coated with a hydrophilic cross-linked polymer to form a support material useful for applications of gas chromatography, supercritical fluid chromatography, solid phase extraction, fluidized beds, and the like. These hydrophilic polymer coatings are formed from monomers or oligomers which comprise polar groups such as sulfonic acids, carboxylic acids, amino groups, phenolic groups, or quaternary ammonium groups. A preferred method to prepare such a coating comprises adsorbing a polymerizable monomer or oligomer onto the surface of the spherules, and cross-linking the monomer or oligomer. See G. Schomberg, LC-GC, 6, 36 (1988).

The present polymer-coated particles can also be combined with a suitable binder and used to coat a glass or plastic substrate to form plates for thin-layer chromatography.

In addition to their utility in chromatographic applications, the present polymer-coated carbon-clad inorganic oxide particles may be useful as an adsorptive medium in non-chromatographic applications. For example, the particles may be utilized as an adsorptive medium in batch adsorbers, fluidized bed adsorbers, membrane adsorbers and the like. The particles may also be useful as an adsorptive medium in pressure-swing adsorption apparatuses. In addition, the present particles may be useful as support materials for fixed bed reactors, batch reactors, fluidized bed reactors and the like.

Therefore, a preferred embodiment of the present invention is a chromatographic support material comprising carbon-clad inorganic oxide particles having a cross-linked outermost coating of a polymer thereon, wherein the polymer-coated particles preferably have a pore size from about 50-1000 Å, a surface area of about 2-80 m^2/g, and an average diameter of about 2-1000 µ. As used herein, "polymer coating" means that the carbon-clad surface of the particle is substantially covered with a layer of an organic polymer. Preferred embodiments of the particles will comprise about 0.1-10 mg polymer per square meter of the surface of the carbon-clad particles. Since spherically shaped particles are desirable for packing into liquid chromatography columns, a preferred embodiment of the present polymer-coated support material comprises substantially spherical particles, or "spherules."

The scope of the present invention is also intended to encompass polymer-coated, carbon-clad particles which are essentially non-porous. Prior to carbon cladding, preferred non-porous inorganic oxide substrate particles will have a diameter of about 0.4-7 microns, a surface area of about 0.1-3 m^2/g, and negligible internal porosity, although the particles may have surface roughness. Useful non-porous inorganic oxides having the preferred diameter and surface area values can be prepared by methods well known to those of ordinary skill in the art of ceramic powder preparation. The polymer-coated, carbon-clad non-porous particles are believed to be particularly useful as a stationary phase support material in liquid chromatography separations of large molecules such as proteins and polymers. The large size of such molecules can hinder or prohibit their rapid diffusion in and out of pores of a porous support material.

Advantageously, the present polymer-coated, carbon-clad support material displays a remarkable stability over a wide pH range, and can be used for the chromatographic separation of compounds at their optimal pHs. For example, the carbon-clad, polymer-coated material prepared according to the invention can be used for the separation of amines at a variety of pHs and mobile phase conditions so that the separation occurs either by a reversed-phase retention mode, a cation-exchange mode, or some combination of the two. For example, at high pH (e.g., pH = 12), the amines are unprotonated so that separation occurs entirely by a reversed-phase mode. At low pH, in the presence of a low ionic strength phosphate buffer and with an organic solvent-rich mobile phase, the separation can occur via a cation-exchange mode if the polymer coating contains cation exchange groups, e.g., carboxylic or sulphonic acid groups. By adjustment of mobile-phase conditions, selectivity can thus be significantly enhanced.

Another advantage of the present polymer-coated, carbon-clad material is that various desired surface chemistries can be imparted to the material by the cross-linking of a variety of polymers on the carbon-clad surface and, optionally, chemical derivatization of the polymeric coating. In this manner, stationary phase supports for reversed phase chromatography, hydrophobic interaction chromatography, size exclusion chromatography, affinity chromatography, chiral chromatography and ion exchange chromatography can be realized. The table below lists representative polymer coatings which are suitable for various desired chromatographic characters.

Polymer Chemistries for Different Chromatographic Characters

Desired Chromatographic Character	Recommended Polymer Coating
Reversed Phase	Polybutadiene C_1-C_{18} Derivatized Polymer Polystyrene
Hydrophobic Interaction	Polyvinylalcohol Poly(ethylene glycol) Polyvinylpyrollidone
Ion Exchange	Polyethyleneimine Poly(butadiene maleic acid)
Size Exclusion	Dextran Polyvinylpyrollidone Polyvinylalcohol Polysiloxanes
Affinity Chiral	Affinity Ligands Attached to N-Acryloxysuccinimide Poly-ℓ-Histidine

The present invention further provides a method for forming a polymer-coated support material useful as a stationary phase in liquid chromatography. The method includes the steps of (a) providing a plurality of inorganic oxide particles comprising a surface which is substantially covered by a carbon cladding; (b) coating the carbon-clad particles with a monomer or oligomer; and (c) cross-linking the monomer or oligomer to form a plurality of polymer-coated, carbon-clad particles. In a preferred application, the method includes an additional step of exposing the carbon-clad particles to a gaseous reducing mixture comprising hydrogen prior to coating them with the monomer or oligomer. This exposure is intended to cause reduction of polar oxygenated sites which may remain exposed on the particles' surfaces following the application of the carbon layer. The carbon-clad inorganic oxide particles to be polymer coated in application of the present method may have a porous surface or may be essentially non-porous.

Detailed Description of the Invention

The present invention provides both a composite material useful as a chromatographic support, and a method for forming a chromatographic support material.

The present material comprises a particle, preferably a spherical particle or "spherule", comprising a core, base or substrate of a porous zirconium oxide, and a cladding of carbon over the porous core. Because an intended use of the present support material is in liquid chromatography applications, it is preferred that the individual units of the material be spherical in shape, in order to permit optimal packing into a column. Therefore, as used herein with respect to the present support material, a "spherule" refers to a substantially spherical particle. Accordingly, as used herein, a "diameter" of a unit of the present support material refers to the average lateral dimension or "particle size" across the particle, but is not intended to imply that the particle is a perfect sphere. The words "spherule" and "particle" are intended to be used interchangeably hereinafter, as are the words "diameter," "size" and "particle size." The present invention is also intended to encompass irregularly shaped particles, which may be useful, e.g., in low performance chromatography, fluidized beds, and general batch absorbers.

The diameter of the core ZrO_2 particles may vary within ranges appropriate for the desired use of the particles. Generally in sorbent applications, ZrO_2 particles of up to about 1 cm in size are preferred. For liquid chromatography applications, preferred core ZrO_2 spherules range in size from about 1 - 500 μ, and more preferably, about 2-50 μ.

The criteria for utility of a particular material as the core or substrate of the carbon-clad particles are that the base material, preferably in the form of a spherule, possesses a high total surface area and thus good sorption capacity, and that this surface area is not excessively reduced during the carbon cladding and any other subsequent coating or cladding procedure included within the scope of the present invention. Therefore, useful surface areas for the core ZrO_2 particles range from about 5 - 300 m^2/g, more preferably about 15 - 100 m^2/g.

The carbon-clad ZrO_2 particles are preferably prepared by a low pressure chemical vapor deposition (CVD) method, discussed below. Therefore, the pore diameter of the base material must be sufficiently large to permit ready diffusion of hydrocarbon vapor into the pores of the core ZrO_2 particle during the CVD. Thus, preferred pore sizes for the core ZrO_2 particles range from about 20 - 5000 Å, more preferably about 60 - 1000 Å.

The zirconium oxide cores are clad or coated with a layer of pyrolytic carbon. Terms related to carbon and its formation are discussed and defined in 9 The Chemistry and Physics of Carbon 173-263 (P. Walker et al., eds. 1973), the disclosure of which is incorporated by reference herein. For example, at pages 174-175, the authors disclose that "pyrolytic carbon" and "CVD carbon" are generic terms relating to the carbon material that is deposited on the substrate by the thermal pyrolysis of a carbon-bearing vapor. The term "CVD carbon" describes the processing used, whereas the term "pyrolytic carbon" refers more to the type of carbon material that is deposited. The authors further disclose that the process of depositing pyrolytic carbon in porous substrates is generally referred to as "infiltration."

While any method of applying pyrolytic carbon to a porous substrate can be used in the preparation of the carbon-clad zirconia, it is preferable to apply the carbon cladding in a manner which results in substantial carbon coverage of the porous ZrO_2 surface. Our method, detailed below, employs a low pressure chemical vapor deposition technique to substantially clad a porous inorganic oxide particle. For example, by utilizing the method, a carbon cladding can be applied which covers greater than 98% of the total exposed surface of a porous zirconia particle, within a time period of about 30 minutes and at a deposition temperature of about 700 °C, when toluene is used as the carbon source.

The carbon-clad ZrO_2 support material is useful in at least two fields:

First, the carbon-clad ZrO_2 material is useful as a stable reversed-phase chromatographic support material. Advantageously, the selectivity for polarizable solutes and hydroxyl solutes can be exploited to separate these species. The loading capacity of the support for these species can be adjusted, if required, by proper selection of the support material (i.e., pore size and specific surface area) and column size (overall capacity).

Second, the carbon cladding is useful as a covering or masking agent for the ZrO_2 surface. ZrO_2 surfaces are known to interact strongly with carboxylic acids, sulfonates, phosphates, and the like. These interactions can lead to undesirable behaviors in chromatography applications. Although some residual ZrO_2 sites may still remain exposed after the carbon cladding, substantially all of the surface is covered with a carbon cladding whose retentivity can be controlled more easily than the retentivity of bare ZrO_2. Improvement of the coating and/or optimization of the pore geometry together with this technology may be used to produce a uniform hydrophobic coating to "seal" the ZrO_2 surface.

There is significant solvent selectivity involved in the use of the carbon-clad ZrO_2 for chromatography. The choice of solvent may also affect the level of solute loading which can be practically employed.

I. Sources of Zirconium Oxide

Preferably, the core ZrO_2 particles will be spherules formed from a ZrO_2 sol. In this embodiment, a portion, or more preferably a majority, of the initial ZrO_2 used to form the core spherules will be in the sol state; i.e., a colloidal dispersion of ZrO_2 particles in water. Once the water is removed, the sol particles interact strongly with one another to provide aggregated sol particles.

Colloidal dispersions of zirconium oxide suitable for use as the ZrO_2 source in preparation of the spherules include the Nyacol™ Zr series, Nyacol, Inc., Ashland, MA. These dispersions contain about 20 wt-% ZrO_2, wherein the ZrO_2 particles vary in average diameter, e.g., from about 10-200 nm. For example, Nyacol™ Zr 100/20 is an aqueous dispersion containing 20 wt-% ZrO_2 of colloidal ZrO_2 particles, the majority of which are about 100 nm in diameter.

Non-colloidal ZrO_2 sources may be included along with the colloidal ZrO_2 dispersions as useful starting materials for these spherules. Thus, chloride, nitrate, sulphate, acetate, formate or other inorganic or organic salts of zirconium such as the oxysalts and alkoxides may be included with the ZrO_2 sol and the mixture used to make spherules. Preferably, colloidal ZrO_2 particles make up the major portion of the total ZrO_2 present in the mixture.

Organic compounds may also be included with the ZrO_2 sources used to prepare the spherules. These organic materials are removed during the firing of the spherules. In particular, water-soluble polymers such as polyvinylpyrrolidone, polyethylene glycol, polyethylene oxide, and the like, or latex particles may be included in the liquid mixture used to prepare the spherules. These materials may act to alter the rheology of the precursor solution, or the pore structure of the resulting fired spherule.

The core ZrO_2 spherules can comprise a minor amount of other metal oxides in addition to ZrO_2. For example, precursors for other metal oxides may be included with the ZrO_2 precursors, so as to stabilize a particular crystalline phase of ZrO_2 or to retard grain growth in the fired spherules. Thus, salts or sols of metals such as yttrium, magnesium, calcium, cerium, aluminum, and the like may be included in levels of from approximately 0-20 mole-%. ZrO_2 spherules which do not contain other oxide additives and are fired in air or in oxidizing atmospheres display either monoclinic, tetragonal or pseudocubic crystal structures when cooled to room temperature. Higher firing temperatures and longer firing times favor the formation of the monoclinic phase. The inclusion of other metal oxides allows the preparation of spherules which possess either monoclinic, tetragonal, or cubic crystalline structures.

These features of ZrO_2 are well known in the art and are discussed in, for example, An Introduction to Zirconia, Magnesium Elektron Ltd., Twickenham, England (2d ed., Magnesium Elektron Publication No. 113, July 1986).

II. Preparation of Core ZrO_2 Spherules

Where the core zirconium oxide spherules are to be formed from a ZrO_2 sol, an aqueous sol containing a colloidal dispersion of ZrO_2 particles can be dispersed in a medium which will extract water from the dispersed sol in the form of droplets. Removal of all or a portion of the water results in gelled solid spherules which consist of aggregated sol particles. One extracting medium which may be used is 2-ethyl-1-hexanol, as disclosed in U.S. Patent No. 4,138,336. A preferred extracting medium for safety reasons and ease of processing is peanut oil, which is preferably used at a temperature of about 80-100 °C. The most preferred extracting medium is a mixture of peanut oil and oleyl alcohol, which are combined in a ratio of about 1:1 and used at a temperature of about 80-100 °C. Oleyl alcohol possesses a higher extraction capacity than peanut oil, and mixtures of the two allow the extraction capacity of the medium to be controlled. Depending upon the ratio of sol to forming medium, extraction times of from about 1-60 minutes can be used to fully gel the ZrO_2 particles. The gelled spherules may be conveniently separated from the extracting medium by any suitable method, e.g., by filtration.

The spherules may also be prepared by the process of spray drying, as disclosed, for example, in U.S. Patent No. 4,138,336.

Once the ZrO_2 particles are condensed into spherules in the above manner, thermal treatment at firing temperatures of from about 100-1500 °C, preferably about 400-800 °C, is performed. The resulting fired spherules are preferably from about 1-500 μ in diameter, and preferably possess a surface area of 5-300 m^2/g and pore diameters of about 20-5000 Å.

III. Low Pressure CVD Method

Either porous or essentially non-porous inorganic oxide spherules can be employed as the substrate material. Advantageously, both the interior and the exterior surfaces and the surfaces of any open pores of the inorganic oxide substrates treated in accordance with this method can be substantially covered with a cladding of carbon. By "low pressure," it is meant that the pressure of the vaporized carbon source in the deposition chamber will be preferably less than about 50 Torr, and more preferably less than about 20 Torr. Since the system pressure in the deposition chamber prior to introduction of the vaporized carbon source will preferably be less than about 10 Torr, the total pressure during the deposition will preferably be less than about 60 Torr, and more preferably less than about 30 Torr.

The preferred temperature to be maintained during deposition of carbon ranges from about 500-1500 °C, and more preferably is about 600-1000 °C. The preferred deposition time is from about 1 minute - 4 hours (240 minutes), but more preferably is between 15 minutes -1 hour. It is believed that the method advantageously provides inorganic oxide spherules with a much more complete and uniform surface coverage in a shorter period of time than conventional CVD techniques.

The inorganic oxide spherules which are preferably utilized in the method will have a diameter of about 1 - 500 microns, a surface area of about 5 - 300 m^2/g, and, if porous, a pore diameter of about 20 - 5000 Å. Although any inorganic oxide meeting these criteria may be employed as a core or substrate material in practice of the method, preferred inorganic oxides include those commonly employed in sorbent applications, e.g., SiO_2, TiO_2, Al_2O_3, MgO, and ZrO_2. Suitable SiO_2 spherules are commercially available under the trade name HPLC Silica Nucleosil, from Macherey-Nagel (Germany). For liquid chromatography applications, a metal oxide which displays a relatively high resistance to dissolution in aqueous media is preferably employed. Suitable metal oxides in this group include, but are not limited to, Al_2O_3, TiO_2, HfO_2 or ZrO_2, with ZrO_2 and HfO_2 being most preferred metal oxides because of their high resistance to

dissolution. Suitable Al_2O_3 spherules are commercially available under the trade name Spherisorb Alumina from Phase Sep, Inc., Hauppauge, New York. Suitable TiO_2 spherules can be prepared as disclosed in United States Patent No. 4,138,336. Compounds or mixtures of more than one inorganic oxide may also be employed in the method as the core or substrate material.

Any carbon source which can be vaporized and which will carbonize on the surface of the inorganic oxide substrate under the temperature and pressure of the method may be employed to deposit a carbon cladding via CVD. Useful carbon sources include hydrocarbons such as aromatic hydrocarbons, e.g., benzene, toluene, xylene, and the like; aliphatic hydrocarbons, e.g., heptane, cyclohexane, substituted cyclohexane butane, propane, methane, and the like; unsaturated hydrocarbons; branched hydrocarbons (both saturated and unsaturated), e.g., isooctane; ethers; ketones; aldehydes; alcohols such as heptanol, butanol, propanol, and the like; chlorinated hydrocarbons, e.g., methylene chloride, chloroform, trichloroethylene, and the like; and mixtures thereof. Another useful carbon source may be a gaseous mixture comprising hydrogen and carbon monoxide, as described by P. Winslow and A. T. Bell, J. Catalysis, 86, 158-172 (1984), the disclosure of which is incorporated by reference herein.

The carbon source may be either a liquid or a vapor at room temperature and atmospheric pressure although it is employed in the CVD process in vapor form. If the carbon source is a liquid with low volatility at room temperature, it may be heated to produce sufficient vapor for the deposition.

In general, the choice of the optimum deposition temperature, pressure and time conditions are dependent on the carbon source employed and the nature of the metal oxide. For example, higher hydrocarbon vapor pressures, higher deposition temperatures and longer deposition times will generally lead to increased amounts of carbon being deposited. Higher deposition temperatures and higher total pressures will, however, also result in a greater tendency for deposition to be localized on or near to the peripheral surface of the substrate particles. If such increased deposition on the exterior surface restricts access of the hydrocarbon vapor to the surfaces of the pores of the particle, these internal surfaces may be poorly coated and therefore their chromatographic performance impaired. Furthermore, the restricted access to the pores may also reduce the chromatographic utility of the particle. Thus, it is preferable to optimize deposition conditions so that the carbon cladding substantially and evenly covers both the external surface and the surfaces of the pores, and does not restrict the subsequent access of hydrocarbon to the surface of the pores. This condition is favored by lower deposition temperatures, e.g., 500 - 1000 °C and lower total pressures, e.g., 1 - 50 Torr. Since lower deposition temperature and pressure results in a slower rate of carbon deposition, longer deposition times will be employed in order to deposit a layer of carbon adequate to cover the surface of the particle. Therefore, the optimum conditions may require a compromise between degree of surface coating and length of deposition time. Advantageously, the method results in substantially complete surface coverage of the inorganic oxide spherules, i.e., at least about 75%, preferably at least about 90%, and more preferably at least about 95% of the surface will be covered.

A suitable apparatus for carrying out the method utilizing chemical vapor deposition is shown schematically in Figure 1 by reference numeral 10. In an application of the method, a sample 12 of inorganic oxide spherules is placed in sample boat 14, and centrally positioned within a tubular reaction chamber 16 (cross-section not shown). Tubular reaction chamber 16 is situated substantially cocentrically within tubular furnace 18, which has a first end 20 and a second end 22. Tubular furnace 18 also includes means for maintaining the sufficiently high temperature, e.g., 500-1500 °C, within the tubular furnace, for chemical vapor deposition.

Connected to both first end 20 and second end 22 of tubular reaction chamber 16 are end fittings 24. The end fitting 24 connected to second end 22 is an "O"-ring joint which provides means for connecting second end 22 to a winch 26, while end fitting 24 connected to first end 20 of tubular reaction chamber 16 is an "O"-ring joint which provides means for connecting first end 20 to an inner quartz tube 28. After chemical vapor deposition is completed, sample 12 in sample boat 14 may be removed from reaction chamber 16 without breaking a vacuum seal by means of an arrangement consisting of a temperature-resistant thread 32 connected to winch 26.

The pressure within tubular reaction chamber 16 can be reduced to below atmospheric pressure by means of vacuum system, shown generally as reference numeral 30. The pressure may be measured by vacuum sensor 40 and indicated by vacuum gauge 42, or by any other suitable means. In more sophisticated apparatuses, it is envisioned that a feedback control system could receive an input signal from vacuum sensor 40 and would control pressure by adjusting the vacuum pump operation accordingly. Additionally, means of monitoring the flow of vapor into the reaction chamber would be provided. Preferably, means for agitating the sample of spherules during the deposition process would be provided to ensure more thorough coating uniformity.

Inner quartz tube 28 is connected to vacuum tubing 34 which is in turn connected to a flask 36 containing a carbon source 38. The temperature of carbon source 38 is maintained by a water bath in which flask 36 is immersed or by other suitable means known in the art. It is preferred that the carbon source 38 and the water of the water bath are both stirred to maintain a constant temperature. Carbon source vapor is carried through vacuum tubing 34 and inner quartz tube 28 into reaction chamber 16, where it decomposes upon contact with sample 12 maintained at an elevated temperature, e.g., 500-1500 °C, within the reaction chamber. Thus, a thin cladding of carbon is deposited on the surface of the porous inorganic oxide spherules of sample 12.

After their preparation the carbon-clad spherules may be packed into a chromatography column and used to perform liquid chromatographic separations. Conventional slurry packing techniques can be employed to pack LC columns with the spherules. For a general discussion of LC techniques and apparatuses, see Remington's Pharmaceutical Sciences, A. Osol, ed., Mack Publishing Col, Easton, PA (16th ed. 1980), at pages 575-576, the disclosure of which is incorporated by reference herein.

IV. Polymer-Coated Carbon-clad Inorganic Oxide Particles

A. Polymerizable Monomers or Oligomers

A wide variety of cross-linkable organic materials, which may be monomers, oligomers or polymers, can be employed to coat the carbon-clad inorganic oxide particles. For example, such materials include polybutadiene, polystyrene, polyacrylates, polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), polyorganosiloxanes, polyethylene, poly(C_1-C_4)alkylstyrene, polyisoprene, polyethyleneimine, and polyaspartic acid.

A preferred material for the preparation of a reversed-phase support material is the oligomer precursor of a hydrophobic polymer such as polybutadiene. A preferred material for modification of the spherules to form a cation ion exchange support is polyaspartic acid.

B. Cross-linking Agents

Any of the common free radical sources including organic peroxides such as dicumyl peroxide, benzoyl peroxide or diazo compounds such as 2,2'-azobisisobutyronitrile (AIBN) may be employed as cross-linking agents in the practice of the present invention. Useful commercially available peroxyesters include the alkylesters of peroxycarboxylic acids, the alkylesters of monoperoxydicarboxylic acids, the dialkylesters of diperoxydicarboxylic acids, the alkylesters of monoperoxycarbonic acids and the alkylene diesters of peroxycarboxylic acids. These peroxyesters include t-butyl peroctoate, t-butyl perbenzoate, t-butyl peroxyneodecanoate and t-butyl peroxymaleic acid. These compounds are commercially available from Pennwalt Chemicals, Buffalo, NY. The amount of any free radical initiator required to catalyze the polymerization reaction will vary depending upon the molecular weight of the initiator and its thermal stability. For typical applications of the present invention, about 2-2.5 g of initiator will be required per 100 g pre-polymer.

Oligomers may also be polymerized by irradiation with UV light or gamma rays or by exposure to high energy electrons.

C. Polymer Coating/Cross-linking Process

Once inorganic oxide spherules have been carbon-clad, the chemical character of the particles (Reversed Phase, Ion Exchange, etc.) can be controlled by coating the particles with a selected pre-polymer. The polymeric coating is generally performed in two steps. First, a pre-polymer is deposited on the surface of the carbon-clad particle. Secondly, the pre-polymer is immobilized by a cross-linking reaction, thereby creating a continuous polymeric coating on the surface of the particle.

The pre-polymer can be deposited on the particle surface in a variety of ways, including pre-polymer deposition by solvent removal, selective adsorption from solution, and gas phase deposition.

When chemical cross-linking agents are used, the cross-linking reaction is preferably carried out under vacuum, to inhibit oxidation of the pre-polymer or polymer. Alternatively, the cross-linking reaction can be carried out in an inert gas, such as nitrogen or helium.

After cooling under a vacuum and rinsing with solvent to remove residual pre-polymer, the resultant polymer-coated particles can be packed into HPLC columns by dry packing or upward slurry packing, depending on their particle size.

The invention will be further described by reference to the following detailed Examples. The Examples are directed to the following subject matter:

Examples 1 - 8	Preparation of Core ZrO_2 Spherules
Examples 9 - 17	Carbon Cladding by Low Pressure CVD Method
Examples 18 - 19	Chromatographic Studies Utilizing Carbon-Clad ZrO_2 as Stationary Phase
Examples 20 - 23	Chromatographic Studies Comparing Silica and Carbon-Clad ZrO_2 Stationary Phases
Example 24	Comparison of Aromatic and Aliphatic Hydrocarbon Carbon Sources for CVD
Example 25	Comparison of Alcohol and Aliphatic Hydrocarbon Carbon Sources for CVD
Examples 26 - 27	Preparation and Evaluation of Polybutadiene-Coated Carbon-Clad ZrO_2 Spherules

Example 1 Preparation of Core ZrO_2 Spherules.

Peanut oil (3 liters) was placed in a 4 liter beaker and heated to 90 °C. A mechanical agitator was inserted and the peanut oil was vigorously stirred. One hundred grams of Nyacol™ Zr 95/20, a colloidal ZrO_2 manufactured by Nyacol, Inc., Ashland, MA, and containing 20 wt-% of ZrO_2, primarily as about 95 nm particles, was sprayed into the peanut oil through an aerosol atomizer. After approximately 30 minutes, the batch was filtered through a No. 54 Whatman filter. Approximately 17 g of solids were recovered, which were predominately spherules having a diameter of < 30 μ.

Example 2.

Preparation of Core ZrO_2 Spherules

Peanut oil (600 g) and 600 g of oleyl alcohol were mixed and heated to about 90 °C. Under vigorous agitation, 100 g of Nyacol™ Zr 95/20 was sprayed into the peanut oil/oleyl alcohol mixture as described in Example 1. After 30 minutes, the batch was filtered and the particles collected. The particles were predominately (ca: 70%) spherules having a diameter of < 50 μ.

Spherules prepared as described in Examples 1 and 2 were thermally treated at a series of temperatures and the surface area, average pore diameter and pore volume as a percentage of total volume were measured by nitrogen adsorption isotherm on a Quantasorb surface area analyzer. These results are summarized in Table 2-1, below.

Table 2-1

Physical Characteristics of ZrO_2 Spherules			
Firing Temp (°C)*	Surface Area (m^2/g)	Average Pore Diameter (Å)	Pore Volume (%)
400	142	42	47
500	92	71	50
600	34	110	36
800	17	205	34
900	14	220	31

* 6 hrs

The data summarized in Table 2-1 show that it is possible to increase the average pore diameter by increasing the firing temperature from 400 to 900 °C. The surface area and pore volume decrease with increasing firing temperature. Since chromatographic capacity of the ZrO_2 spherules is determined by the surface area, average pore diameter and pore volume, the appropriate firing temperature can be selected to control these parameters.

Example 3.

Preparation of Core ZrO_2 Spherules

The procedure of Example 2 was employed to prepare spherules using Nyacol™ Zr 50/20, a colloidal ZrO_2 supplied by Nyacol, Inc. (50 nm ZrO_2 colloidal size) as the ZrO_2 source.

Example 4.

Preparation of Core ZrO_2 Spherules

The procedure of Example 2 was used to prepare spherules using Nyacol ™ Zr 150/20, a colloidal ZrO_2 supplied by Nyacol, Inc. (150 nm ZrO_2 colloid size) as the ZrO_2 source.

Table 4-1 summarizes the surface area, average pore diameter and pore volume of spherules prepared as per Examples 2-4 and fired at 600 °C for 6 hrs.

Table 4-1

Physical Characteristics of ZrO_2 Spherules				
ZrO_2 Source* (%)	ZrO_2 Colloid Size (nm)	Surface Area (m^2/g)	Average Pore Diameter (Å)	Pore Volume
Zr 50/20	50	33	92	31
Zr 95/20	95	34	110	36
Zr 150/20	150	40	147	45

* Nyacol™ series.

The data summarized in Table 4-1 show that it is possible to control the average pore diameter of the fired spherules by appropriate selection of the colloid size of the ZrO_2 source. Larger colloids produce fired spherules with larger pore diameters and pore volumes.

Example 5.

Preparation of Core ZrO_2 Spherules with Single Centrifugation

Nyacol™ Zr 95/20 colloidal ZrO_2 was placed in a laboratory centrifuge and sedimented. The supernatant was decanted and discarded. The sedimented ZrO_2 was redispersed in an equal volume of distilled water. Spherules were prepared from this centrifuged sol following the procedures of Example 2.

Example 6.

Preparation of Core ZrO_2 Spherules with Double Centrifugation

The centrifugation procedure of Example 5 was performed and the redispersed sol was subsequently recentrifuged to sediment, the supernatant decanted off and the ZrO_2 redispersed. Spherules were prepared from this doubly centrifuged sol following the procedure of Example 2.

Example 7.

Preparation of Core ZrO_2 Spherules with Triple Centrifugation

The double centrifugation procedure used in Example 6 was performed and the redispersed sol was subsequently recentrifuged to sediment, the supernatant decanted and the ZrO_2 redispersed. Spherules were prepared from this triply centrifuged sol following the procedures of Example 2.

Table 7-1 summarizes the surface area, pore diameter and pore volume of spherules prepared as per Examples 2, 5, 6 and 7 and heated to 600 °C for 6 hrs.

Table 7-1

Physical Characteristics of ZrO_2 Spherules			
ZrO_2 Source *	Surface Area (m^2/g)	Average Pore Diameter (Å)	Pore Volume (%)
Zr 95/20	34	110	36
Zr 95/20 cent. (1x)	50	162	55
Zr 95/20 cent. (2x)	52	235	62
Zr 95/20 cent. (3x)	46	250	62

* Nyacol™ Zr series.

Centrifugation, removal of the supernatant, and redispersion of the colloidal ZrO_2 starting material results in increases in the average pore diameter, pore volume and surface area of fired spherules. This increase is believed to result from the removal of small (ca. 5-10 nm) colloidal ZrO_2 particles which are known to be present in the Nyacol™ Zr series sols as a minor component. Many of these smaller ZrO_2 particles remain suspended during centrifugation and are removed when the supernatant is discarded prior to redispersion of the larger sedimented ZrO_2 particles. If present, these small ZrO_2 particles are believed to increase the packing density of the spherules by filling the interstices between larger ZrO_2 particles and therefore decreasing the average pore diameter, pore volume and surface area of the fired spherules.

It is also possible that sedimentation by centrifugation may result in agglomeration of the colloidal ZrO_2 particles into aggregates which pack together in a more open structure (effectively behaving as larger particles) than unaggregated particles.

Regardless of mechanism, the centrifugation treatments described in Examples 5-7 provide a method of preparing spherules with increased average pore diameter, pore volume and surface area relative to spherules prepared from untreated colloidal ZrO_2 sols.

Example 8.

Preparation of Core ZrO_2 Spherules With Spray Drying

Preparation A

A 4500 g sample of Nyacol™ Zr 100/20, which contained 20 wt-% ZrO_2 primarily as about 100 nm particles, was concentrated on a rotary evaporator until its concentration was 35% ZrO_2 by weight. This sol was then spray dried on a spray drier manufactured by Nyro Incorporated. About 900 g of dried solids were obtained. When examined under an optical microscope, the solids were observed to be spherules from about 0.5 to 30 μ in diameter. The dried spherules were fired by heating them in a furnace to a temperature of 600°C over 6 hours, with additional heating applied at a constant temperature of 600°C for 6 more hours. Nitrogen adsorption measurements on the fired ZrO_2 spherules indicated that their average surface area was 48.1 m^2/g and their average pore diameter was 116 Å. The spherules were air classified, and the fraction ranging in size from approximately 5-10 μ was subsequently used for chromatography experiments.

Preparation B

To prepare spherules with larger diameter pores than those of Preparation A, the procedure described below was followed. 1200 g of Nyacol™ Zr 100/20 colloidal ZrO_2 were centrifuged on a laboratory centrifuge at 5000 rpm for 55 minutes. The supernatant was discarded and the sediment was re-dispersed in distilled water. The centrifuged sol was placed on a rotary evaporator and concentrated until it contained 35% by weight of ZrO_2. Following spray drying of the sol under conditions similar to those described in Preparation A, about 300 g of dried solids were obtained. When examined under an optical microscope, the solids were observed to be spherules ranging in size from about 1 to 30 μ in diameter. Many of the spherules (>50%) were observed to possess cracks, especially those spherules of larger size. A portion of the fired spherules was then placed in a furnace and heated to a temperature of 1100°C over 9 hours, with additional heating at a constant temperature of 1100°C for 6 more hours. The surface area of the fired spherules was determined to be 16.1 m^2/g, and the average pore diameter was 408 Å, as measured by mercury porosimetry. This technique is a preferred method for measuring the size of pores greater than about 250 Å in diameter. The fired spherules were unchanged in appearance from the dried spherules.

They were nearly all intact, but many (>50%) were cracked.

A portion of the fired spherules was classified by size fraction as described in Preparation A. Examination of the classified fractions indicated that a portion of the spherules had fractured during the classification procedure. Many intact spherules remained, but a portion of each fraction contained irregularly shaped particles which appeared to have been produced by the fracturing of the spherules during the classification process.

Preparation C

To prevent the cracking observed in the spherules prepared according to Preparation B, spherules were also prepared as follows: 1250 g of Nyacol™ Zr 100/20 colloidal ZrO_2 were placed in a laboratory centrifuge and spun at 5000 rpm for 55 minutes. The supernatant was discarded and the sediment was re-dispersed in distilled water. This centrifuged sol was placed on a rotary evaporator and concentrated until the concentration of ZrO_2 in the sol was 32 wt%. To 513 g of this sol were added 34.6 g of a solution of zirconyl acetate containing 25% by weight ZrO_2 equivalent (Harshaw, Inc., Cleveland, Ohio), and 61 g of a solution containing 50 wt% PVP K30, a polyvinylpyrrolidone polymer (GAF Corporation, Texas City, Texas) were added to the concentrated sol. The resulting mixture was then agitated rapidly into a 50/50 mixture of peanut oil and oleyl alcohol which had been heated to a temperature of 90°C. The resulting mixture contained gelled spherules of about 1 to 30 μ in diameter, which were observed under an optical microscope to be intact and crack-free.

The spherules were then fired to a temperature of 900°C over 7 hours and 20 minutes, with heating at a constant temperature of 900°C for an additional 6 hours. After firing, the resulting spherules were from about 1 to 25 μ in diameter, and were observed under an optical microscope to be intact and crack-free. The surface area and average pore diameter of these microspheres were measured by mercury porosimetry to be 28 m^2/g and 415 Å, respectively. A portion of these spherules was classified into 5-10 μ and 10-20 μ fractions by sieving. Following classification, the classified spherules remained uncracked and intact.

Example 9.

Chemical Vapor Deposition of Carbon on Core ZrO_2 Spherules (Toluene as Carbon Source)

In order to deposit a thin film or cladding of carbon over the zirconia substrate, "bare" or unclad ZrO_2 spherules were treated as follows.

15 g of porous ZrO_2 spherules, prepared according to the procedure of Example 8A above, which had a diameter of about 8 u and a surface area of 56.5 m^2/g and an average pore diameter of 90 Å, were placed in a ceramic sample boat. The boat was placed in a reaction chamber within a small tube furnace similar to that shown in Figure 1. The vacuum pump of the system was engaged, and the total system pressure was lowered to about 1 Torr (1 mm mercury). The furnace was then heated to a temperature of 700°C. After equilibrating at 700°C for about 1 hour, the valve to the flask containing toluene at 22°C was opened slightly, allowing toluene vapor to enter the reaction chamber. With this valve open, the total pressure in the system rose to about 8 Torr, as measured by the vacuum gauge. This gauge is calibrated to measure N_2 partial pressures. The effect of measuring the pressure of vapors such as toluene on the accuracy of the gauge is not known, but the gauge was used as a means of measuring the relative pressures used in the preparation of samples, instead of absolute pressures. The limits on the pressure of toluene are 0 Torr with the valve closed, to 23 Torr, which is the vapor pressure of toluene at 22°C. The pressure was maintained at a gauge reading of about 8 Torr for 10 minutes. During this time, the originally white ZrO_2 spherules turned black in color due to the deposition of carbon on their surfaces.

After 10 minutes of deposition, the boat was removed from the furnace but kept in the reaction chamber under vacuum by using a winch as shown in Figure 1 to pull the sample from the furnace. After a cooling time of about 15 minutes, the spherules were removed from the reaction chamber and inspected. By visual observation, the spherules were free-flowing and undamaged by the low pressure CVD treatment. The specific surface area and average pore diameter of the spherules were measured and found to be 38.7 m^2/g and 113 Å, respectively.

Example 10.

Effect of Varying Deposition Time at 700 °C

This example describes an experiment designed to determine the effect of deposition time on amount of carbon deposited and spherule surface area under constant deposition conditions. Four tests were completed in which samples of ZrO_2 spherules underwent CVD of carbon for 5, 10, 20 and 25 minutes, respectively. Each of the four samples consisted of 4 g of porous ZrO_2 spherules, prepared according to the procedure of Example 8A above, having a particle size of about 1 - 10 u and a surface area of 48 m^2/g. Each sample was placed in a sample boat similar to that shown in Figure 1, which was then placed in the reaction chamber that had been heated to 700 °C in the tubular furnace according to Example 9. The system pressure was lowered to about 2 Torr by operation of the vacuum pump. After equilibrating for 10 minutes, the valve to the flask containing toluene was opened slightly, thus allowing toluene vapor to enter the reaction chamber, until the total system pressure rose to a vacuum gauge reading of about 5 Torr. This valve setting and temperature were maintained for the varying lengths of time shown in Table 10-1 below. Each sample was then removed from the furnace, but kept within the reaction chamber under vacuum until the sample had cooled, about 15 minutes. After cooling, the surface area and the weight percent carbon and hydrogen of each sample were measured, and are listed below in Table 10-1.

TABLE 10-1

Deposition Time (min.)	Surf. Area (m^2/g)	Wt% C	Wt% H
5	50	1.4	0.1
10	45	3.7	0.1
20	34	5.4	0.2
25	36	6.8	0.2

These results show that at a constant deposition temperature and pressure, the weight percent of the carbon coating increases, and the surface area, in general, decreases with increasing deposition time.

Example 11.

Effect of Varying Deposition Time at 775 °C

This example describes the effect of varying the deposition time at 775 °C, at a toluene vapor pressure of about 23 Torr as measured by a vacuum gauge, on the surface area of ZrO_2 spherules. 5 g of ZrO_2 spherules prepared according to Example 2 and fired to 600 °C, and having a surface area of 61 m^2/g and an average pore diameter of 96 Å, were placed in a sample boat which was placed in the reaction chamber as described in Example 10, with the exception that the temperature was maintained at 775 °C. The pressure of the system was reduced to about 4 Torr with the vacuum pump, and the system allowed to equilibrate for about 10 minutes. When the valve leading to the flask which contained toluene was opened, the total system pressure as measured by the vacuum gauge rose to about 27 Torr due to the presence of the toluene vapor. On contact with the heated sample, the toluene vapors decomposed, resulting in the deposition of a carbonaceous layer on the ZrO_2. Following decomposition for the times shown in Table 11-1 below, the samples were removed from the furnace but left in the reaction chamber under vacuum by winching from the furnace. After cooling in the quartz tube under vacuum for about 15 minutes, the surface area and average pore diameter of each sample was measured. Table 11-1 shows the results of these experiments.

TABLE 11-1

Deposition Time (min.)	Surf. Area (m^2/g)	Avg. Pore Dia. (Å)
2	38	112
5	38	102
10	31	101

The data in Table 11-1 show that the surface area and the average pore diameter of the pores decreases with increasing deposition time.

Example 12.

Effect of Varying Deposition Temperature and Pressure

This example describes the deposition of the carbon layer at different conditions of temperature and toluene partial pressure. Two samples, each comprising 8 g of porous ZrO_2 spherules prepared according to Example 8A above, were placed in a sample boat that was placed in the reaction chamber maintained at the deposition temperatures shown in Table 12-1 below. The system pressure was then lowered with the vacuum pump to about 2 Torr. After equilibrating the system for 10 minutes, the valve to the toluene flask was opened, thus allowing toluene vapor to enter the reaction chamber. Deposition continued for the times shown in Table 12-1. After cooling under vacuum for about 15 minutes, the surface area, weight percent carbon, and weight percent hydrogen of each sample were measured, and are listed in Table 12-1 below.

TABLE 12-1

Temp. (°C)	Time (min.)	Surf. Area (m^2/g)	Wt% C	Wt% H
1000	8	6.5	8.1	0.1
500	17	46.0	0.5	0.1

By visual observation, the 1000°C sample was black in color, while the 500°C sample was tan in color. During deposition at 1000°C, a black deposit was also noted on the exit end of the reaction chamber. This experiment showed that the rate of carbon deposition increases with increasing deposition temperature.

Example 13.

Preparation of Carbon-Clad SiO_2 and Al_2O_3 Spherules (Toluene as Carbon Source)

This example describes treatment of porous SiO_2 and Al_2O_3 spherules by the low pressure CVD method to prepare carbon-clad SiO_2 and Al_2O_3. The base silica spherules employed were HPLC Silica Nucleosil, from Macherey-Nagel (Germany) which had a 15 - 25 u particle size. The base alumina spherules employed were SPHERISORB ALUMINA, obtained from Phase Sep Inc., Hauppauge, New York, which had about a 10 u particle size. For each of three tests, a 0.9 g sample of spherules was placed in a sample boat and the boat was positioned in the quartz tubular reaction chamber at the selected temperature shown in Table 13-1 below. The pressure in the reaction chamber was reduced to 5 Torr with a vacuum pump, and the system was allowed to equilibrate for 10 minutes. The valve to the flask containing the toluene carbon source was then opened and the total pressure raised to a vacuum gauge reading of about 9 Torr due to the introduction of the toluene vapor. After deposition for the time periods indicated in Table 13-1 below, each sample was allowed to cool under vacuum for about 15 minutes and its surface area, weight percent carbon and weight percent hydrogen were measured. The results are listed in Table 13-1, below.

TABLE 13-1

Sample	Temp. (°C)	Time (min.)	Color	Surf. A (m^2/g)	Wt% C	Wt% H
SiO_2	700	10	white	103	0.4	<0.1
SiO_2	800	10	black	80	2.0	<0.1
Al_2O_3	700	10	black	113	4.2	0.6

The results indicate that the low pressure CVD method is useful for carbon cladding other inorganic oxides besides ZrO_2. However, the data of Table 13-1 indicate that a higher temperature (i.e., greater than 700°C) may be required to effect equivalent levels of carbon deposition from toluene onto SiO_2, than the temperature required to effect carbon deposition onto Al_2O_3 or ZrO_2 (less than or up to about 700°C).

Example 14.

Reductive Treatment of ZrO_2 Carbon-clad Spherules

This example describes heat treatment of carbon-clad ZrO_2 spherules prepared according to Example 9 while exposing them to a reducing atmosphere. The purpose of the heat treatment was to cause the reduction of polar functional groups on the carbon-clad surface of the spherules, thereby modifying chromatographic performance by increasing the homogeneity of the surface of the spherules.

A 20 g sample of carbon-clad ZrO_2 spherules prepared according to Example 9 (toluene hydrocarbon source) was placed in an Al_2O_3 sample boat inside of a mullite tubular reaction chamber with gas tight seals on both ends. The reaction chamber was then placed within a tubular furnace, in accordance with the arrangement depicted in Figure 1. The sample of ZrO_2 spherules was exposed to a gaseous reducing mixture of 95% Ar/5% H_2 by flowing this mixture through the reaction chamber. After allowing the system to equilibrate for about 30 minutes, the sample was heated to a temperature of 700°C over 2 hours, and thereafter maintained at 700°C for an additional hour. At the end of the third hour, the furnace was shut off and the samples allowed to cool in the tube, still under the flow of 95% Ar/5% H_2.

Example 15.

Use of n-Heptane as Carbon Source

This example describes the use of n-heptane, rather than toluene, as the carbon source for the present low pressure CVD process. A 9 g sample of ZrO_2 spherules prepared according to Example 8A, which had a diameter of about 5 u, a surface area of 40 m^2/g, and an average pore diameter of about 164 Å, were placed in a sample boat similar to that shown in Figure 1. The boat was positioned in the quartz tubular reaction chamber as in the previous Examples. The system was equilibrated at a temperature of 700°C and a pressure of about 1 Torr for 10 minutes. The valve to the flask containing n-heptane was then opened slightly, bringing the total system pressure to about 5 Torr as measured by the vacuum gauge, due to the presence of n-heptane vapor. These conditions were maintained for 20 minutes before the sample was winched from the furnace and allowed to cool under vacuum for about 15 minutes. By visual observation, the clad spherules ranged from dark grey to black in color. It was also observed that the portion of the sample located nearer to the top of the sample boat was darker in color than the portion of the sample below.

Example 16.

Effect of Reheated Carbon-cladding

This example describes experiments in which a thin cladding of carbon was deposited on a sample of ZrO_2 spherules as described in the previous examples, the carbon-clad sample was mixed or stirred up, and additional carbon was then deposited by repeating the CVD in order to improve coating homogeneity.

A sample of ZrO_2 spherules prepared according to Example 8A, which had a diameter of about 5 u, a surface area of 40 m^2/g, and an average pore diameter of 164 Å, were heated to a temperature of 700°C, and held at this temperature for 6 hours prior to the cladding procedure. Two tests were performed, one employing toluene as the carbon source, the other using n-heptane. The amount of carbon source

vaporized during each test was determined by weighing each flask at the beginning and the end of each test. The temperature maintained in the furnace during each test was 700 °C, and in both tests the original system pressure was about 6 Torr. Each sample underwent carbon vapor deposition for 15 minutes, cooling for 15 minutes, thorough mixing of the sample, and a second carbon vapor deposition for another 15 minutes. After cooling for about 15 minutes following the second carbon deposition, the surface area, weight percent carbon, and weight percent hydrogen of each sample were analyzed, and are listed in Table 16-1 below.

TABLE 16-1

CARBON % SOURCE	WEIGHT VOLATILIZED	SURFACE AREA (m^2/g)	WEIGHT % C	WEIGHT H
n-Heptane	6.5 g	24	1.1	<0.1
Toluene	12.5 g	25	3.1	<0.1

Example 17.

Determination of Exposed Zirconia

A technique was developed to determine the amount of bare ZrO_2 remaining exposed, i.e., not clad with carbon, after carrying out the CVD process on ZrO_2 spherules. The technique is based on the known strong adsorption of phosphate ions on ZrO_2 surfaces. More specifically, the amount of remaining exposed zirconia was determined by monitoring phosphate removal from a solution in contact with the carbon-clad zirconia spherules as follows:

In a static adsorption study, a 0.1 g sample of carbon-clad spherules which had been prepared according to Example 9 above was placed in a clean 30 ml polyethylene bottle. A 2 mM to 10 mM standard solution of phosphate was prepared from phosphoric acid and water having a resistivity of greater than 16 megaohms. Twenty ml of the phosphate solution were added to the polyethylene bottle, and a vacuum was applied with sonication to completely wet the pores of the spherules. The mixture of spherules in phosphate solution was then agitated every 30 min for the next 6 to 8 hours. Following agitation, the mixture was allowed to stand for 20-24 hours. At the end of the standing period, the phosphate solution was removed from the polyethylene bottle with a 10 ml glass syringe and passed through a 0.2 um filter to remove any remaining zirconia particles.

The filtered solutions and blanks (standard phosphate solutions) were analyzed for phosphorous using Inductively Coupled Plasma Spectroscopy (ICPS). The amount of phosphorous that had adsorbed to the spherules was determined by the difference between phosphate concentration in the standard solutions (blanks) and the filtered solutions. The ICPS analysis indicated that 90-95% of the surface area of the ZrO_2 substrate had been blocked from interaction with the phosphate solute by the carbon coating.

An additional technique used to determine the carbon coverage of the ZrO_2 spherules involved observation of the breakthrough of a UV-active organophosphate compound such as phenylphosphate through a chromatographic column.

Example 18.

Analysis of Carbon-clad ZrO_2 Spherules

A. Column Packing

A 5 x 0.46 cm HPLC column was packed with the carbon-clad ZrO_2 spherules of Example 9 (toluene carbon source) using an upward slurry technique. This technique involved the use of (i) a first slurry solvent such as hexane or tetrahydrofuran (THF) to suspend the packing material; and (ii) a relatively viscous, miscible solvent such as isopropanol or methanol to displace the slurry into the column. In this manner, the column could be tightly packed at a relatively low flow rate, e.g., up to about 5 ml/min, once the column bed had been established. The column was packed at a pressure of about 6000-9000 psi. Utilization of the lower flow rate (5 ml/min) at these pressures advantageously avoided any significant amount of solvent consumption.

B. Chromatographic Nature

In order to test the chromatographic nature of the carbon-clad support material a chromatographic study was performed using a 5 x 0.46 cm HPLC column packed with the carbon-clad ZrO_2 spherules of Example 9 (toluene carbon source) as the stationary phase. A 70/30 (% v/% v) tetrahydrofuran/water solution at 35 °C was used as the mobile phase.

A 5 µl sample of a mixture of alkylbenzenes was injected onto the packed HPLC column. The resulting chromatogram is shown in Figure 2a. After completion of the separation of the alkylbenzenes, a 5 µl sample of a mixture of alkylphenones was also separated on the column, under identical conditions. The resulting chromatogram is shown in Figure 2b. Capacity factors (i.e., the ratio of solute concentration in the stationary phase to solute concentration in the mobile phase) were calculated for each solute by evaluating the ratio $(t_r - t_o)/t_o$, where t_r is retention time measured at peak maximum, and t_o is column dead time measured by solvent mismatch.

Figure 3 depicts a plot of logarithm of the capacity factor k' vs. carbon number of the components of the alkylbenzene mixture (ethylbenzene through hexylbenzene) (designated by the open circles; m = 0.107, b = - 0.305) and for the components of the alkylphenone mixture (acetophenone through hexanophenone) (designated by the solid circles; m = 0.143, b = - 0.203). As depicted in Figure 3, the points for the homologous series fall on a straight line; the alkylphenones are more retained that the alkylbenzenes; and the slope of the log k' vs. carbon number line for the alkylphenones is slightly greater than that for the alkylbenzenes. These results indicate that the carbon-clad spherules employed as the stationary phase act as a reversed phase material. More specifically, the reversed phase character of the spherules is demonstrated by (i) the linear relationship between logarithm of the capacity factor, k', and the number of methylene groups for a homologous series of solutes; and (ii) the decreasing retention of those solutes as the mobile phase organic modifier concentration was increased.

The greater retention of the alkylphenones than the alkylbenzenes indicates the strong interaction of the carbon-clad ZrO_2 with polarizable compounds, especially aromatic polarizable compounds. The greater retention of the alkylphenones than the alkylbenzenes is the converse of what is observed with bonded phase reversed phase liquid chromatography (RPLC) supports. However, greater retention of alkylphenones than alkylbenzenes is observed on carbon-based supports such as graphitized and pyrolytic carbon.

C. Alkaline Stability

The alkaline stability of carbon-clad ZrO_2 spherules prepared according to Example 9 was tested by repeatedly injecting varying amounts of a test solute, benzene, into a 12.5 x 0.46 cm HPLC column packed with the spherules. A continuous flow of hot alkaline mobile phase of 50% methanol/50% pH 12 water was maintained through the column at a temperature of 80 °C and a flow rate of 0.5 ml/min. During the 60 hour study, a total of 2 liters of the alkaline mobile phase passed through the column. As shown in Figure 4 (capacity factor vs. column volumes), the retention of benzene was quite constant under these conditions.

After completion of the chromatographic stability tests, the packing was removed from the column and analyzed for carbon, hydrogen, and nitrogen content. The results of the CHN analysis, depicted in Table 18-1 below, indicate that essentially none of the carbon was lost from the surface of the packing during the alkaline stability study. Thus, the CHN results confirm the results of the chromatographic stability tests.

Table 18-1

CHN Analysis Results[2]			
Source	%C	%H	%N
Column Front	3.3	0.2	<0.1
Column End	3.4	0.2	<0.1
Column Middle	3.3	0.2	<0.1
Fresh[1]	3.4	0.2	<0.1

[1]Fresh = not exposed to alkaline conditions.
[2]Precision of this analysis was ± 0.1%.

Example 19.

Exposure of CVD Carbon-Clad ZrO_2 Particles to Reducing Conditions

A. Reduction of Polar Surface Groups

An experiment was performed to examine the effect on chromatographic performance of the carbon-clad (toluene carbon source) ZrO_2 spherules when the spherules were exposed to reducing conditions. A 30 g sample of carbon-clad ZrO_2 spherules was prepared, and immediately thereafter exposed to a 95% argon/5% hydrogen atmosphere at a temperature of 700°C for 60 minutes, as described in Example 14. These conditions were expected to reduce the number of polar oxygenated sites which may be present on the carbon surface.

B. Chromatographic Nature of Reduced Material

The reduced material was then packed into a 15 cm x 0.46 cm HPLC column with which several chromatographic studies were carried out. Packing was performed by means of the upward slurry technique described in Example 18. Separations were performed of a mixture of alkylphenones and a mixture of alkylbenzenes, using the reduced, carbon-clad zirconia as the stationary phase and a mobile phase of 70% THF/30% water. Figure 5 depicts a plot of log(capacity factor) vs. carbon number for each alkylphenone component (designated by the solid circles; m = 0.116, b = - 0.056) and alkylbenzene component (designated by the open circles; m = 0.107, b = - 0.217) of the mixture.

Figure 5 indicates that the reduced, carbon-clad stationary phase was operating in reversed-phase mode, since the points for both homologous series fall on a straight line, and the capacity factors increase upon lowering the concentration of organic modifier in the mobile phase. Comparison of Figure 5 with Figure 3 indicates that reductive treatment of the carbon-clad ZrO_2 had little effect on capacity of the material to retain alkylbenzenes, but had a significant effect on the capacity of the material to retain alkylphenones. The slope of the log(capacity factor) vs. carbon number line for alklyphenones is less in Figure 5 than in Figure 3, and more closely approximates the slope of the log(capacity factor) vs. carbon number line for alkylbenzenes. These trends indicate that some of the exceptionally strong adsorption sites on the carbon surface were quenched by the reductive treatment.

In an additional experiment, the efficiency of the HPLC column, packed with the reduced carbon-clad ZrO_2 prepared as described in part A, was compared to the efficiency of a column packed with unreduced carbon-clad ZrO_2, prepared as described in Example 9. Butyrophenone was injected at a reduced velocity of 20, and a 60% THF/40% water mobile phase was maintained at 35°C in both columns. The results indicated that chromatographic efficiency increased by 200% when the reduced support material was used as the stationary phase instead of the non-reduced support material.

In conclusion, these studies showed that the carbon-clad ZrO_2 spherules are a useful reversed phase support and show strong retention of nonpolar solutes and superior alkaline stability and solute selectivity. Furthermore, exposure of the carbon-clad coated ZrO_2 spherules to reducing conditions prior to their utilization in separations improves the efficiency of those separations.

Example 20.

Preparation of Carbon-Clad ZrO_2- and Silica-Packed HPLC Columns

Carbon-clad ZrO_2 spherules prepared according to Example 9 above, but with a 15 minute deposition time, were evaluated as a chromatographic support material. The spherules had a ca 5 µm particle diameter, 100 Å mean pore diameter, and a specific surface are of ca 50 m^2/g.

The carbon-clad ZrO_2 support was packed into a 10 x 0.21 cm equipped with Kel-F encased 2 mm o.d. SS frits by the upward slurry packing technique described in Example 18. Two grams of the support material were slurried and outgassed under vacuum in 17.5 ml of a 5:1 (v/v) hexane/1-octanol solution. The resulting slurry was used to pack the column at 6000 psi using practical grade hexane as solvent. The packed column was subsequently washed with 2-propanol (IPA) and acetonitrile (ACN), and was equilibrated with water/acetonitrile (HOH/ACN) mobile phase for characterization in reversed-phase chromatography.

A 10 x 0.2 cm commercial Hypersil (silica) ODS (C18) column was obtained from the Hewlett-Packard Company, Avondale, Pa.

Example 21.

Comparison of Solute Retention with Varying Organic Mobile Phase Modifier Concentration on Carbon-Clad ZrO_2- and and Silica-Packed Columns

In order to evaluate the nature of solute retention on the carbon-clad ZrO_2 stationary phase of Example 20, the isocratic elution of a mixture of alkyl benzene solutes was analyzed while employing HOH/ACN mobile phases of varying ACN concentration. The sample mixture of alkyl benzenes included benzene, toluene, ethyl benzene, n-propyl benzene, and n-butyl benzene (0.8 mg/ml each in 3/2 methanol/water). One microliter injections of the sample were performed into mobile phase compositions of 65/35, 60/40, 55/45, 50/50, 45/55, 40/60, 35/65, and 30/70 v/v HOH/ACN at a flow rate of 0.500 ml/min while the column was thermostated at 40 °C. Chromatographic characterization was performed on a Hewlett-Packard model 1090M HPLC system equipped with a 0.6 cm pathlength diode array absorbance detector. The elution of the solutes was detected by absorbance at 215 nm. The peak maximum in the absorbance trace was taken as the retention time for each solute in each mobile phase.

For comparison, the same set of injections were made under identical conditions using the commercial Hypersil ODS (C18) column described in Example 20.

A comparison of the actual retention time data for the alkyl benzenes on the carbon-clad ZrO_2-packed column with that of the solutes on the traditional silica-based commercial Hypersil ODS (C18) column is shown in Table 21-1 below:

TABLE 21-1.

RETENTION OF ALKYL BENZENES AS A FUNCTION OF % ORGANIC:

solute	65/35 W/A ZrO_2	65/35 W/A SiO_2	60/40 W/A ZrO_2	60/40 W/A SiO_2	55/45 W/A ZrO_2	55/45 W/A SiO_2	50/50 W/A ZrO_2	50/50 W/A SiO_2
BENZENE	1.84	2.65	1.45		1.17	1.60	0.990	1.32
TOLUENE	3.69	4.79	2.56		1.91	2.42	1.493	1.85
ETHYL BENZENE	5.75		3.69		2.57	3.71	1.893	2.66
PROPYL BENZENE	13.80		7.82		4.96	6.14	3.370	4.12
BUTYL BENZENE	> 20		17.50		10.26	10.28	6.443	6.48

solute	45/55 W/A ZrO_2	45/55 W/A SiO_2	40/60 W/A ZrO_2	40/60 W/A SiO_2	35/65 W/A ZrO_2	35/65 W/A SiO_2	30/70 W/A ZrO_2	30/70 W/A SiO_2
BENZENE	0.87	1.11	0.78	0.95	0.71	0.84	0.657	0.758
TOLUENE	1.21	1.48	1.03	1.21	0.89	1.03	0.799	0.897
ETHYL BENZENE	1.47	2.00	1.19	1.56	1.01	1.28	0.871	1.071
PROPYL BENZENE	2.41	2.91	1.83	2.16	1.44	1.69	1.192	1.356
BUTYL BENZENE	4.31	4.34	3.06	3.06	2.27	2.28	1.762	1.742

"W" = water

"A" = acetonitrile

The results shown in Table 21-1 indicate that the retention of n-butyl benzene is virtually identical on both columns. For the remaining alkyl benzene solutes (ethyl through butyl), the retentions on the two phases are roughly comparable.

Example 22.

Comparison of Capacity Factor for Separations with Carbon-Clad ZrO_2-Packed HPLC Column and Silica-Packed Column

The retention characteristics of several substituted benzene solutes were compared during isocratic reversed-phase chromatography on the carbon-clad ZrO_2-packed column and the commercial Hypersil ODS column of Example 20. 0.2 µl injections of the alkyl benzene solute solution into a 2/1 water/ACN (1/1 water/ACN for iodobenzene) mobile phase were made for each of the columns, and equilibrated with 65/35 v/v water/ACN at 0.500 ml/min and 40 °C. The concentration of solute in the samples was 1-4 ppt (mg/ml or µl/ml). Absorbance was detected at both 215 nm and 260 nm. The dead volume characteristics of both of the columns were probed by injectioning solutions of deuterium oxide (D_2O)/ACN and dilute solutions of uracil and of sodium nitrate.

The capacity factors (k') for the various solutes were calculated from the retention times (tR) after correction for the experimentally determined extracolumn dead volume of 35 µl, based on approximate dead volumes of 200 µl and 150 µl for the carbon-clad ZrO_2 column and the Hypersil column, respectively. The capacity factors are listed in Table 22-1 below:

TABLE 22-1.

COMPARISON OF CARBON CLAD ZIRCONIA WITH COMMERCIAL C18 SILICA

Solute	mg/ml mg/ml	Solvent	5 mm CARBON-CLAD ZrO_2 tR	5 mm CARBON-CLAD ZrO_2 k'	HYPERSIL 5 mM C18 SiO_2 tR	HYPERSIL 5 mM C18 SiO_2 k'
			0.40		0.30	
D_2O			0.55	0.19	0.37	-0.01
ACETONITRILE (CH_3CN)			0.54	0.17	0.46	0.30
URACIL ($C_4H_4N_2O_2$)	1.2	H_2O	0.98	1.29	0.39	0.08
PHENOL (C_6H_5OH)	4.4	2/1 W/A	1.33	2.15.	0.92	1.82
ANILINE ($C_6H_5NH_2$)	3.3	2/1 W/A	1.45	2.45	1.32	3.17
BENZENE (C_6H_6)	3.3	2/1 W/A	1.83	3.39	2.65	7.61
m - CRESOL ($C_6H_4CH_3OH$)	3.3	2/1 W/A	2.19	4.30	1.22	2.82
p - CRESOL ($C_6H_4CH_3OH$)	3.3	2/1 W/A	2.23	4.39	1.18	2.70
FLUORO BENZENE (C_6H_5F)	3.3	2/1 W/A	2.25	4.45	2.88	8.35
o - CRESOL ($C_6H_4CH_3OH$)	3.3	2/1 W/A	2.51	5.11	1.32	3.18
BENZONITRILE (C_6H_5CN)	3.3	2/1 W/A	3.07	6.51	1.57	4.00
BENZALDEHYDE (C_6H_5CHO)	3.3	2/1 W/A	3.60	7.82	1.31	3.13
TOLUENE ($C_6H_5CH_3$)	3.3	2/1 W/A	3.61	7.85	4.79	14.72
CHLORO BENZENE (C_6H_5Cl)	3.3	2/1 W/A	5.42	12.37	4.88	15.03
m - XYLENE (C_8H_{10})	3.3	2/1 W/A	7.02	16.38	8.51	27.14
p - XYLENE (C_8H_{10})	3.3	2/1 W/A	7.99	18.80	8.60	27.44
BROMO BENZENE (C_6H_5Br)	3.3	2/1 W/A	7.19	16.81		
NITRO BENZENE ($C_6H_5NO_2$)	3.3	2/1 W/A	7.78	18.29	2.08	5.71
o - XYLENE (C_8H_{10})	3.3	2/1 W/A	9.73	23.16	7.89	25.06
IODO BENZENE (C_6H_5I)	3.3	1/1 W/A	14.57	35.24	7.65	24.27
BENZOIC ACID (C_6H_5COOH)	3.4	2/1 W/A	>> 20	>> 65	0.54	0.57
Na BENZENE SULFONATE ($C_6H_5NaO_3S$)	3.4	2/1 W/A	>> 20	>> 65	0.33	-0.12

The results shown in Table 22-1 indicate several unique features of the carbon-clad ZrO_2 material. Oxygen-containing solutes (e.g., uracil, phenol, cresols, benzaldehyde, and acids) were significantly more retained on the carbon-clad ZrO_2 material than on the Hypersil (silica) support material. In addition, solutes having strongly dipolar and polarizable groups (e.g., uracil, benzonitrile, benzaldehyde, nitrobenzene, and iodobenzene) were significantly more retained on the carbon-clad ZrO_2 support than on the Hypersil (silica) support. The pure hydrocarbon solutes (e.g., benzene, toluene, xylene) were more strongly retained on the Hypersil (silica) support material than on the carbon-clad ZrO_2 material. The retention of polysubstituted species such as the xylenes and the cresols indicates a geometric dependency on the carbon-clad ZrO_2 material with a retention order of meta < para < ortho. In contrast, the Hypersil (silica) material exhibited

differing retention orders of para < meta < ortho < and ortho < meta < para for the cresols and the xylenes, respectively.

Example 23.

Comparison of Capacity Factor for Carbon-Clad ZrO_2-Packed HPLC Column and Silica-Packed Column under Acidic and Basic Conditions

The retention on the 10 cm x 2.1 mm carbon-clad ZrO_2-packed column of Example 20 was also evaluated under acidic (1% formic acid, HCOOH) and basic (0.10 M sodium hydroxide, NaOH) aqueous solvent conditions. 0.2 µl samples were injected onto the carbon-clad ZrO_2 column, equilibrated with 65/35 aqueous/ACN solvent, were eluted isocratically, and were detected as described above. The results are shown in Table 23-1 below, which lists the retention times of various test solutes for 0.5 ml/min., 40°C mobile phases of 65/35 1% formic acid (HCOOH)/ACN, for 65/35 water/ACN, and for 0.1 M (pH 13) sodium hydroxide (NaOH)/ACN:

TABLE 23-1.

COMPARISON OF RETENTION ON CARBON CLAD ZIRCONIA: pH EFFECTS

5 mm CARBON COATED ZIRCONIA COLUMN:

Solute	mg/ml	Solvent	35/65 ACN/65 1% HCOOH tR	ACN/H_2O tR	35/65 ACN/ 0.1M (pH 13) NaOH tR
SODIUM NITRATE		H_2O		0.72	0.37
D20		--	0.58	0.54	0.44
ACETONITRILE		--	0.58	0.53	0.42
URACIL	1.2	H_2O	0.65	0.98	0.38
PHENOL	4.4	2/1 W/A	1.22	1.32	0.41

The usefulness of the carbon-clad ZrO_2 stationary phase for separations in which either strongly acidic or basic mobile phases are utilized is demonstrated by the retention data in Table 23-1. The results indicate that the retention of solutes with ionizable acidic and basic groups change dramatically with changes in pH of the mobile phase, while the shifts in retention for other solutes are significantly less for the extreme pH mobile phases. Most significantly, solutes such as benzoic acid and benzene sulfonate, which are strongly retained in acidic and neutral solutions, elute in the dead volume of the hydroxide solution. Conversely,

aniline retention drops dramatically in acidic solution relative to neutral or basic mobile phases.

These trends are even more apparent when represented as selectivity values (α) relative to benzene, as shown in Table 23-2 below:

TABLE 23-2.

ALPHA VALUES (RELATIVE TO BENZENE) FOR CARBON CLAD ZIRCONIA

k'(x)/k'(benzene)

			5 mm CARBON COATED ZIRCONIA COLUMN:		
			35/65 ACN/ 1% HCOOH	35/65 ACN/H$_2$O	35/65 ACN/ 0.1M NaOH
Solute	mg/ml	Solvent	tR	tR	tR
URACIL	1.2	H_2O	0.39	0.52	0.26
PHENOL	4.4	2/1 W/A	0.77	0.71	0.28
ANILINE	3.3	2/1 W/A	0.31	0.78	0.70
BENZENE	3.3	2/1 W/A	1.00	1.00	1.00
m - CRESOL	3.3	2/1 W/A	1.21	1.20	0.32
p - CRESOL	3.3	2/1 W/A	1.25	1.22	0.35
FLUORO BENZENE	3.3	2/1 W/A	1.23	1.24	1.24
o - CRESOL	3.3	2/1 W/A	1.41	1.39	0.37
BENZONITRILE	3.3	2/1 W/A	1.81	1.71	1.83
BENZALDEHYDE	3.3	2/1 W/A	2.00	2.00	2.31
TOLUENE	3.3	2/1 W/A	2.09	2.01	1.99
CHLORO BENZENE	3.3	2/1 W/A	3.20	3.04	3.03
ETHYL BENZENE	4	2/1/2 W/A/M	2.94	3.23	3.01
m - XYLENE	3.3	2/1 W/A	3.79	3.96	3.75
p - XYLENE	3.3	2/1 W/A	4.22	4.51	4.26
BROMO BENZENE	3.3	2/1 W/A	4.23	4.05	4.22
NITRO BENZENE	3.3	2/1 W/A	4.47	4.39	4.76
o - XYLENE		2/1 W/A	5.09	5.50	5.29
n-PROPYL BENZENE	4.0	2/1/2 W/A/M	6.76	7.82	6.79
IODO BENZENE	3.3	2/1 W/A	8.28	8.25	7.98
BENZOIC ACID	3.4	2/1 W/A	5.45	-	0.25
Na BENZENE SULFONATE	4	2/1 W/A -	-	0.25	
* assuming VO = 200 ml			3.70	4.38	3.03

Example 24.

Comparison of Toluene and Heptane as Carbon Sources

The following experiments were performed in order to study the effect of varying the carbon source used in the low pressure CVD method on chromatographic performance of the resulting spherules.

Two approximately 5 g batches of carbon-clad ZrO_2 spherules were prepared, one according to the procedure of Example 9 (toluene carbon source), and the other according to the procedure of Example 15 (n-heptane carbon source). Samples from each batch were used as the packing of two 5 X 0.46 cm HPLC columns operated with a 40°C mobile phase of 40% THF and 60% water. The upward slurry packing technique described in Example 18 was used to pack both columns. An identical mixture of ethylbenzene (EtBen) and nitrobenzene (NitroBen) was separated on each column. The results of the separations are shown in Table 24-1 below:

Table 24-1

Comparison of CVD Heptane and CVD Toluene Chromatographic Efficiency				
Flow Rate[1] (ml/min)	CVD Heptane		CVD Toluene	
	h[2]-EtBen	h-NitroBen	h-EtBen	h-NitroBen
1.5	4.5	5.8	14.8	342
1.0	4.3	5.3	13.5	236
0.5	3.6	4.7	15.0	---
0.35	3.6	4.8	14.2	283
0.2	5.6	5.0	19.3	239

[1]flow rate of mobile phase
[2]h = reduced plate height

The high values of reduced plate height, indicating poor chromatographic efficiency, and the weak dependence on flow rate observed in Table 24-1 for the column prepared using toluene as the carbon source, indicate that the reduced chromatographic efficiency is due to chemical processes, instead of sluggish diffusion in micropores or similar physical processes.

Additional separations of a mixture of ethylbenzene, butylphenyl ether, propiophenone, and nitrobenzene were performed on both columns. Capacity factors (k') and reduced plate heights (h) were calculated for each solute, and are shown in Table 24-2 below:

Table 24-2

Chromatographic Separation of Different Solutes on CVD Heptane and CVD Toluene				
Solute	CVD Heptane		CVD Toluene	
	k'	h	k'	h
Ethylbenzene	3.3	4.5	2.4	11
Butylphenyl Ether	10.0	7.4	5.1	28
Propiophenone	3.8	7.6	2.5	120
Nitrobenzene	3.6	5.3	5.5	194

Loading studies of both columns were also performed by calculating the capacity factor, k', for various amounts of sample which were injected onto the columns. A mobile phase of 40% THF/60% water was maintained throughout the study at a temperature of 40°C and a flow rate of 1 ml/min. The sample was an aqueous solution of nitrobenzene, at a concentration of approximately 10 mg nitrobenze/ml solution. The results of the loading studies are shown in Table 24-3 below:

Table 24-3

Comparison of Chromatographic Loading on CVD n-Heptane and CVD Toluene				
Amt Injected (mg)	CVD n-Heptane		CVD Toluene	
	k'	% change	k'	% change
0.01	3.75		13.3	
		1.3		27
0.02	3.70		9.7	
		1.3		36
0.05	3.65		6.2	
		1.4		31
0.10	3.60		4.3	

The results shown in Tables 24-1, 24-2, and 24-3 indicate that the support material prepared by deposition of carbon from thermal decomposition of n-heptane exhibits significantly improved chromatographic efficiency and loading characteristics as compared to the support material prepared from thermal decomposition of toluene. These results also indicate that variation in the carbon source can strongly affect the various chromatographic properties (e.g., retention, capacity, selectivity and efficiency) of the resultant materials. Thus, control and variation of the carbon source material, together with optional reductive treatment as described in Example 14, can provide differing reversed phase materials suitable for differing separation needs.

Example 25.

Use of n-Butanol as Carbon Source

A. Preparation of Carbon-Clad ZrO_2

A 6.04 g sample of ZrO_2 spherules prepared according to Example 8A was placed in a ceramic sample boat which was then centerally located in a deposition chamber maintained at 700°C. With initial system pressure established at 0.95 Torr, n-butanol was released into the chamber until the system pressure as measured by the vacuum gauge had increased to 6 Torr. Pressure was maintained at between 5.5-6.4 Torr throughout the deposition process. After 45 minutes of carbon deposition, the sample was removed from the deposition chamber and allowed to cool under vacuum for 25 minutes. By visual observation, the particles located at the top of the sample boat were very dark in color, but those at the bottom of the sample boat were much lighter, indicating a less complete carbon cladding of these particles. The deposition process was repeated a second time after thorough mixing of the particle bed. During the second deposition process, the system pressure was maintained at a vacuum gauge reading of between 6.5-12 Torr by warming the carbon source flask containing the n-butanol. After 20 minutes of carbon deposition, the sample was removed and allowed to cool under vacuum for 25 minutes.

B. Chromatographic Analysis

The carbon-clad spherules prepared as described in part A above were packed into a 5 x 0.46 cm HPLC column using the upward slurry technique described in Example 18 above. A 50% THF/50% water mobile phase maintained at a temperature of 40°C and a flow rate of 0.35 ml/min was utilized for the separation of a mixture of alkylphenones and alkylbenzenes. The results of the separation are shown in Fig. 6, which depicts a plot of log k' vs. carbon number for each of the alkylphenone (designated by the solid circles; m = 0.193, b = - 0.095) and alkylbenzene (designated by the open circles; m = 0.145, b = - 0.095) solutes present in the mixture. Reduced plate heights were calculated for each solute, and compared with the reduced plate heights calculated for the same solutes separated on a column packed with carbon-clad zirconia prepared by deposition of carbon from n-heptane (see Example 16). This comparison indicated that the chromatographic efficiency of the material prepared with n-butanol is generally greater than that of the material prepared with n-heptane. Table 25-1 lists the reduced plate height values:

Table 25-1

Comparison of CVD n-Butanol and CVD n-Heptane Chromatographic Efficiency		
Solute	CVD n-Butanol h[1]	CVD n-Heptane h
Butylbenzene	4.1	5.8
Butylphenyl Ether	7.4	10.3
Valrophenone	5.0	5.9
Nitrobenzene	5.2	4.7

[1]h = reduced plate height

Example 26.

Polybutadiene-Coated Carbon-Clad ZrO_2 Spherules

In order to improve the efficiency and loading of the support material but retain the shielding of the carbon-clad surface, carbon-clad inorganic oxide particles were coated with a thin layer of polybutadiene polymer as follows:

An 8 g sample of porous carbon-clad ZrO_2 spherules was prepared according to Example 9. Following chemical vapor deposition, the resulting carbon-clad spherules were dried for 8-10 hours in a vacuum oven at 70-100 °C. A surface area measurement of 39.0 m^2/g was obtained. A 1.01% (wt/vol) solution of polybutadiene (PBD) (avg. m.w. 4500, obtained from Aldrich Chemical Co., Milwaukee, WI) pre-polymer was then made in hexane. 20 ml of the PBD/hexane solution were added to the sample of carbon-clad spherules in a 100 ml flask, at 0.7 mg PBD/hexane solution per square meter of total surface area of the carbon-clad spherules to be coated.

Next, the volume of hexane in the PBD prepolymer solution was adjusted to 5 ml of hexane per gram of packing material by adding hexane. The solution was then sonicated for 5 minutes while a vacuum was applied to the reaction flask, in order to ensure that the pores were completely wetted with prepolymer solution. The reaction flask was then capped and shaken gently for 4 hours to allow the prepolymer to diffuse completely into the pores of the carbon-clad material.

At the end of the 4 hours, 2.5 ml of a solution of 53.61 mg dicumyl peroxide (DCP), a free radical initiator, obtained from Pfaltz and Bauer, Waterbury, CT, in 25 ml of hexane, were added to the reaction flask. The flask contents were agitated overnight. Following agitation, the flask was placed in a rotary evaporator and the solvent was slowly evaporated with gentle heating at 35-40 °C under an intermittently applied vacuum. A round-bottomed flask with a side baffle was used when removing the solvent, to facilitate particle bed mixing. In this manner, a thin uniform pre-polymer/initiator film was created on the surface of the spherules.

In order to allow the polymer to more completely coat the surface, the spherules were warmed to 100 °C for 30 minutes. The temperature was then raised to 145 °C for another 30 minutes to activate the cross-linking initiator. The cross-linking reaction was completed by raising the temperature to 155 °C for an additional 4 hours.

The resulting polymer-coated spherules were allowed to cool for 0.5 hour while stored under vacuum. After cooling, the spherules were sequentially rinsed with 100 ml per gram of spherules of each of the following solvents: hexane, dichloromethane, tetrahydrofuran, and finally hexane again, in order to remove any residual unpolymerized prepolymer or initiator from the spherules.

Example 27.

Evaluation of Polymer-Coated, Carbon-Clad ZrO_2 Spherules as HPLC Support

A. Chromatographic Nature

A 4.5 g sample of the carbon-clad, PBD-coated spherules of Example 26 were packed in a 12.5 x 0.46 cm HPLC column using an upward slurry packing technique. 5 µl of a mixture of alkylphenones and alkylbenzenes were injected onto the packed column. A 50% THF/50% water mobile phase was used at 35 °C. Figure 7 depicts a plot of $\log_{10}$(capacity factor, k') vs. carbon number for each alkylphenone

(designated by the solid circles; m = 0.1260, b = - 0.051) and alkylbenzene (designated by the open circles; m = 0.965, b = 0:179) solute. The reversed-phase character of the polymer-coated packing material is demonstrated by the linear relationship between $\log_{10}(k')$ and carbon number of the homologous series of alkylbenzenes and alkylphenones.

Figure 7 also indicates that the alkylbenzenes were retained by this support to a greater extent than were the alkylphenones. This elution order is typical of conventional silanized bonded reversed phase supports, and is in contrast to what was observed with non-polymer-coated, carbon-clad surfaces (see Figure 3). The order of retention shown in Figure 7 indicates that the retention displayed by this support material is primarily due to its polymer coating, rather than to its carbon cladding.

B. Column Efficiency

The efficiency of a 12.5 x 0.46 cm HPLC column packed with the carbon-clad, PBD-coated ZrO_2 spherules prepared according to Part A above, was examined by a flow rate study. Figure 8A, a plot of reduced flow rate vs. reduced plate height, indicates that propylbenzene (solid circles), butylphenyl ether (triangles) and butyrophenone (open circles) exhibited minimum reduced plate heights of 3.5, 4.4 and 15.5, respectively, with the values for propylbenzene and butylphenyl ether lying quite close to the theoretically optimum value of 2-3. In contrast, non-polymer-coated but carbon-clad supports display a significantly reduced efficiency, as indicated by the higher minimum reduced plate heights shown in the flow rate study of Figure 8B, a plot of reduced flow rate vs. reduced plate height. (Butyrophenone is designated by open circles, propylbenzene is designated by solid circles, and butylphenyl ether is designated by trangles.)

C. Loading Capacity

A loading study of a 12.5 x 0.46 cm HPLC column packed with the carbon-clad, PBD-coated spherules according to Part A above was next performed. The solute for this study was butylphenyl ether, and the mobile phase was 50% THF/50% water, maintained at 35 °C and a flow rate of 1 ml/min. Figure 9A depicts a plot of reduced plate height and capacity factor (K prime) vs. solute loading, and indicates that the capacity factor and reduced plate height remained relatively constant over the broad range of loadings examined. At a very high solute loading, the reduced plate height increased slightly. These results demonstrate that the polymer-coated support has a high solute loading capacity. In contrast, non-polymer-coated but carbon-clad supports display a much lower loading capacity under similar conditions, as demonstrated by the decrease in capacity factor with the increase in solute concentration as shown in Figure 9B.

In summary, the results of parts B and C above indicate that the present polymer-coated carbon-clad support has a greater efficiency and sample-loading capacity than a non-polymer-coated but carbon-clad support.

D. Alkaline Stability

A 12.5 x 0.46 cm HPLC column prepared according to Part A above was tested for alkaline stability by flushing the column with a 50%/50% (v/v) methanol/pH 12 aqueous NaOH solution at 80 °C, and monitoring the retention of benzene. A plot of capacity factor (k') vs. column volumes of mobile phase passed through the column is depicted in Figure 10. Figure 10 indicates that retention of solute remained relatively constant over a wide range of volumes of alkaline mobile phase. The scatter of the points between 1000 and 1440 column volumes is due to benzene loss from the sample vial as the experiment progressed. At 1440 column volumes, a new sample of benzene was placed in the autosampler.

The substantially constant capacity factor and reduced plate height over increasing column volumes of alkaline mobile phase shown in the stability study of Figure 10 (plot of column volumes vs. capacity factor) demonstrate the pH stability of the support. If the support was not pH stable, and had begun to dissolve, a very rapid increase in reduced plate height and a drop in capacity factor would have been observed. The carbon analysis results presented in Table 27-1 are a further indication of the pH stability of the support.

Table 27-1

Carbon Analysis Results			
Source	% C	% H	% N
Head of Column	5.3	0.4	<0.1
Middle of Column	5.2	0.4	<0.1
End of Column	5.3	0.4	<0.1
New Column	5.3	0.3	<0.1

E. Chromatogram

A mixture of alkylphenones was separated on a 12.5 x 0.46 cm HPLC column packed with carbon-clad, polybutadiene-coated spherules according to Part A above. A 1.0 ml/min. mobile phase of 50% THF/50% water was used at 35°C. Figure 11 depicts the chromatogram obtained from this separation. The peaks shown in Figure 11 represent, from left to right, propiophenone, butyrophenone, valerophenone, hexanophenone and heptanophenone, respectively.

F. Physical Structure

Figure 12 is a schematic depiction of a porous polymer-coated, carbon-clad ZrO_2 particle of the present invention.

The invention has been described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many variations and modifications may be made while remaining within the spirit and scope of the invention.

Claims

1. A carbon-clad inorganic oxide particle having an outermost cross-linked polymer coating.

2. A polymer-coated, carbon-clad inorganic oxide particle according to claim 1 which has a diameter of about-2-1000 microns, a surface area of about 2-80m²/g, and a pore size of about 50 - 1000 Å.

3. A particle according to claim 1 or 2 wherein the polymer coating is selected from the group consisting of polybutadiene, polyvinylalcohol, poly(ethylene glycol), polyvinylpyrollidone, polyethyleneimine, poly-(butadiene maleic acid), polysiloxane, and poly-ʟ-histidine, and dextran.

4. A particle according to any one of claims 1 to 3 wherein the inorganic oxide is ZrO_2, HfO_2, Al_2O_3, TiO_2, MgO, or SiO_2.

5. A method for forming a support material useful as a stationary phase in liquid chromatography, comprising the steps of:
   (a) providing a plurality of inorganic oxide particles comprising a surface which is substantially covered by a carbon cladding;
   (b) coating the carbon-clad particles with a monomer or oligomer; and
   (c) cross-linking the monomer or oligomer to form a plurality of polymer-coated carbon-clad inorganic oxide particles.

6. A method according to claim 5, further comprising, prior to said step (b), a step of exposing the carbon-clad particles to a gaseous reducing mixture so as to cause reduction of polar oxygenated sites on the surface of the particles.

7. A method according to claim 5 or 6 wherein the said carbon-clad inorganic oxide particles are formed by the steps of:
   (1) placing a plurality of porous inorganic oxide particles having a surface, a diameter of about 1 - 500 microns, a surface area of about 5-300 m²/g, and a pore diameter of about 20 - 5000 Å within a

reaction chamber;
(2) elevating the temperature within the reaction chamber and reducing the pressure within the reaction chamber; and
(3) introducing a vapor comprising carbon into the reaction chamber so as to thermally decompose the vapor and deposit a cladding of said carbon onto the porous particles, substantially covering the surface of the particles.

8. A method according to claim 7, wherein the deposition is carried out for about 1 - 240 minutes and the pressure is reduced to less than about 60 Torr.

9. A method according to any one of claims 5 to 8 wherein the inorganic oxide is ZrO_2, HfO_2, Al_2O_3, TiO_2, MgO, or SiO_2.

10. A chromatographic support material comprising carbon-clad inorganic oxide particles having an outermost cross-linked polymer coating.

11. A liquid chromatographic stationary phase containing as particles carbon-clad inorganic oxide particles having an outermost cross-linked polymer-coating.

12. An adsorptive medium containing particles, which particles are carbon-clad inorganic oxide particles having an outermost cross-linked polymer-coating.

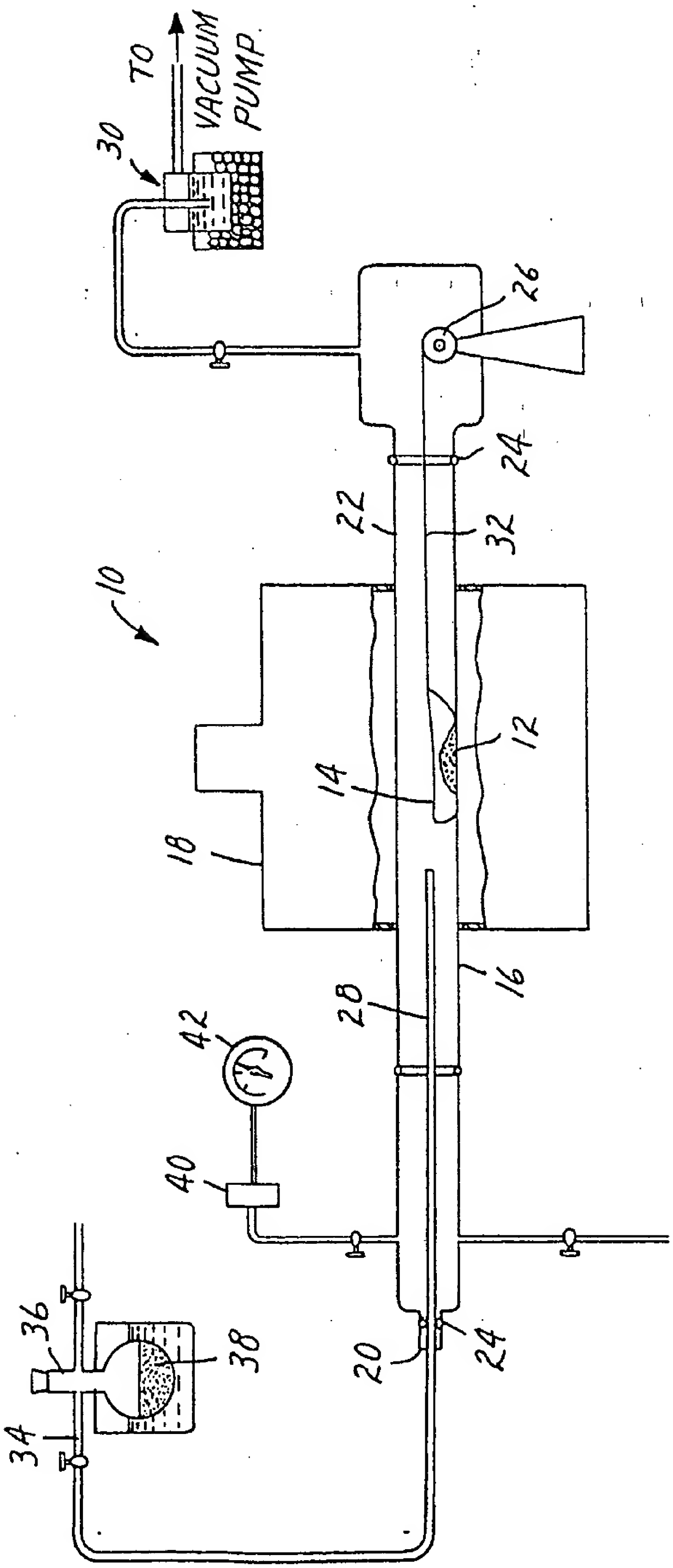


FIG.1

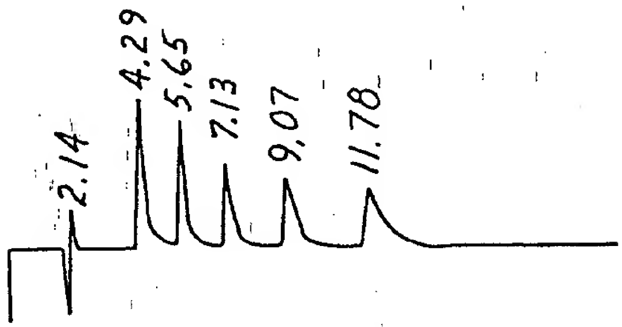


FIG. 2A

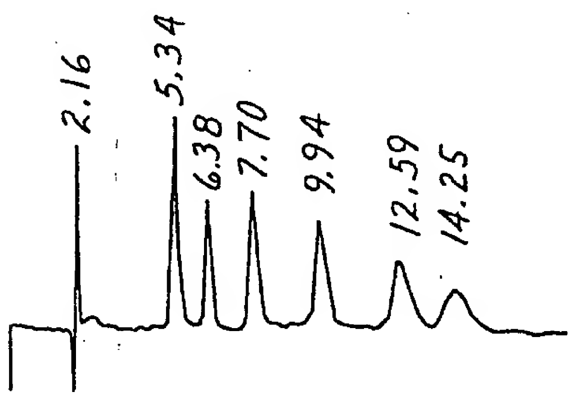


FIG. 2B

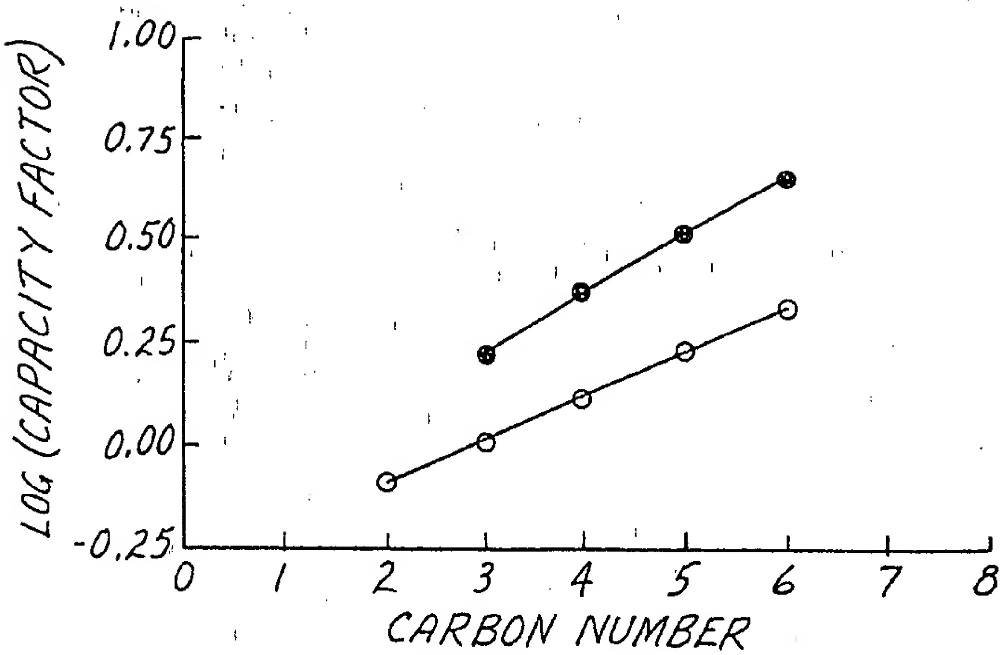

LOG (CAPACITY FACTOR)
1.00
0.75
0.50
0.25
0.00
-0.25
0
1
2
3
4
5
6
7
8
CARBON NUMBER

FIG. 3

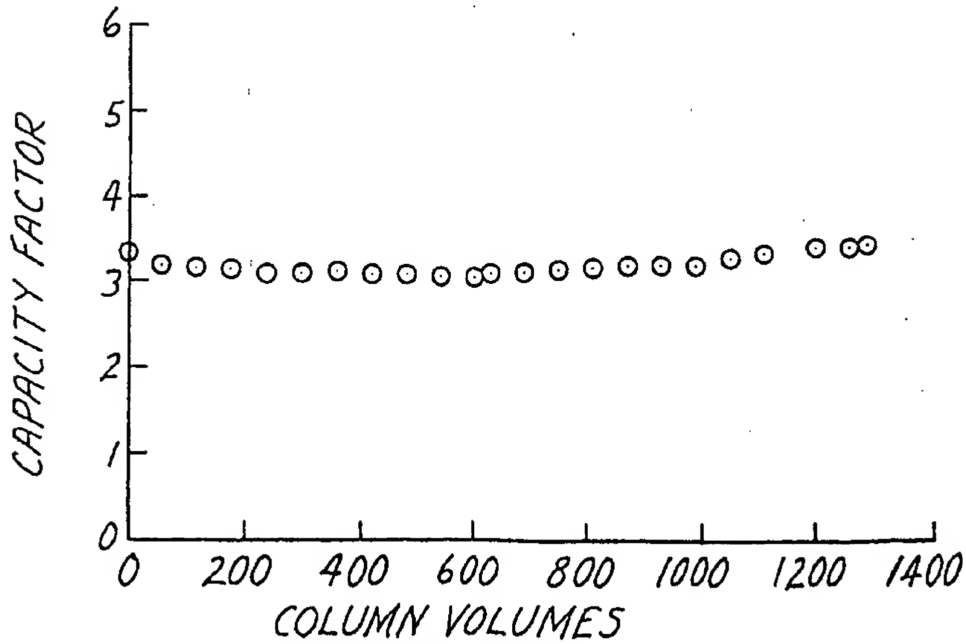

CAPACITY FACTOR
6
5
4
3
2
1
0
0
200
400
600
800
1000
1200
1400
COLUMN VOLUMES

FIG. 4

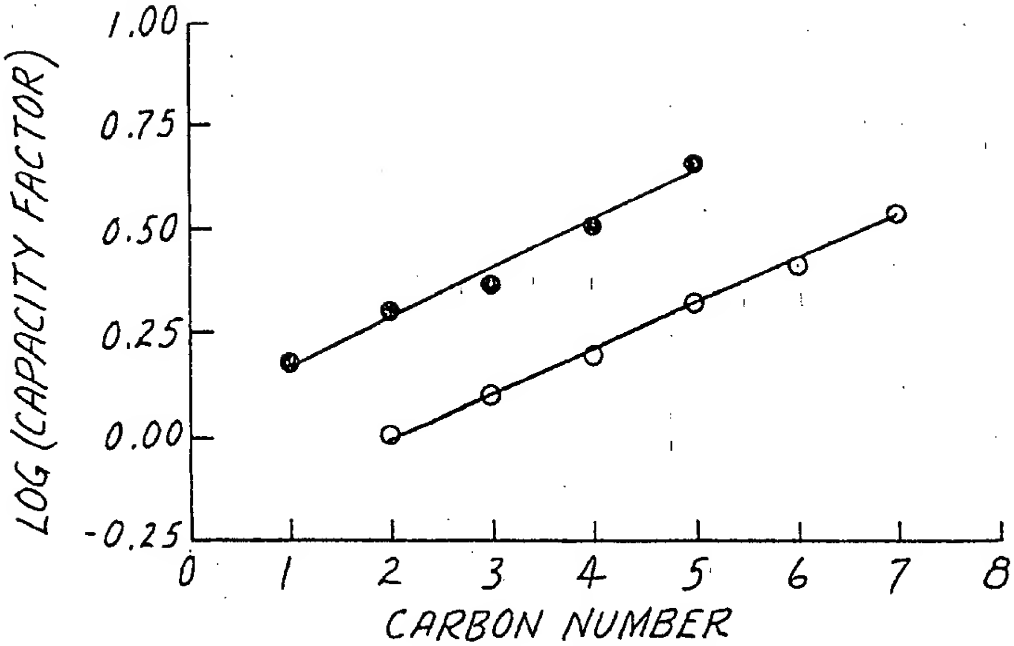

LOG (CAPACITY FACTOR)
1.00
0.75
0.50
0.25
0.00
-0.25
0
1
2
3
4
5
6
7
8
CARBON NUMBER

FIG. 5

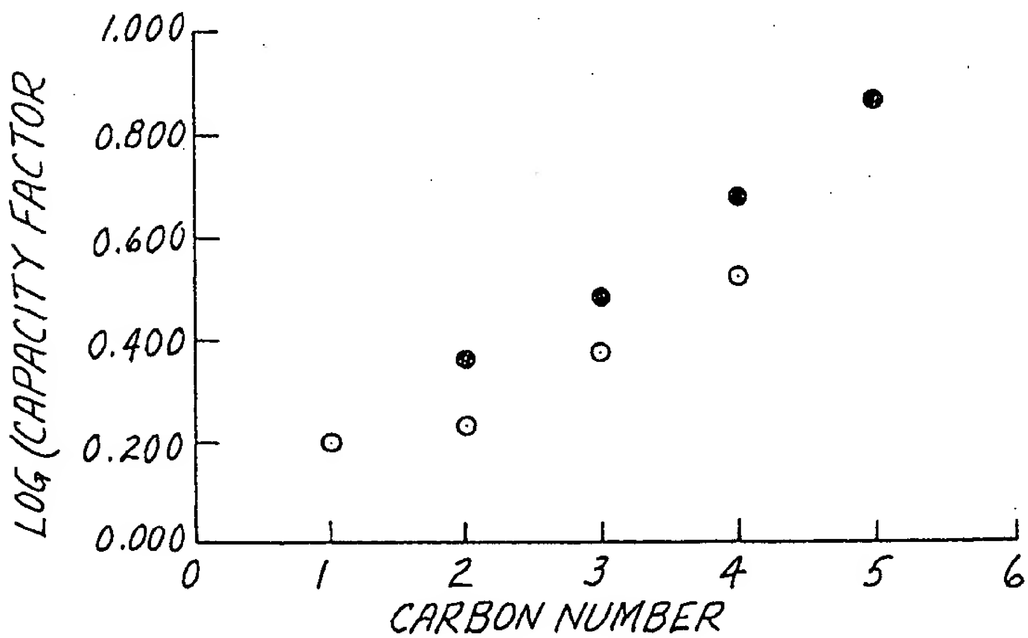

LOG (CAPACITY FACTOR
1.000
0.800
0.600
0.400
0.200
0.000
0
1
2
3
4
5
6
CARBON NUMBER

FIG. 6

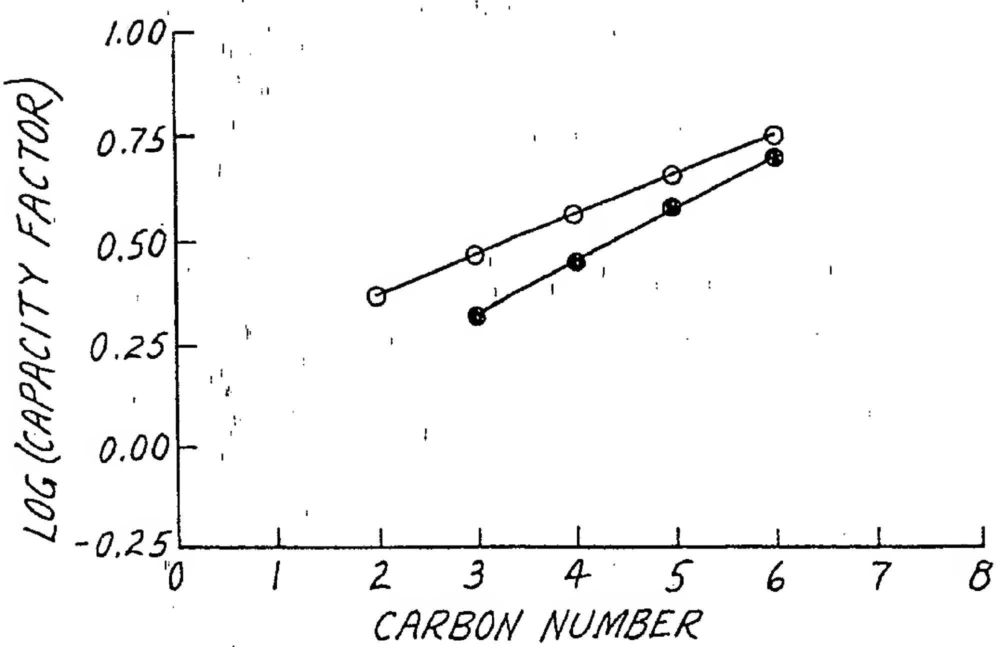

1.00
0.75
0.50
0.25
0.00
-0.25
LOG (CAPACITY FACTOR)
0
1
2
3
4
5
6
7
8
CARBON NUMBER

FIG. 7

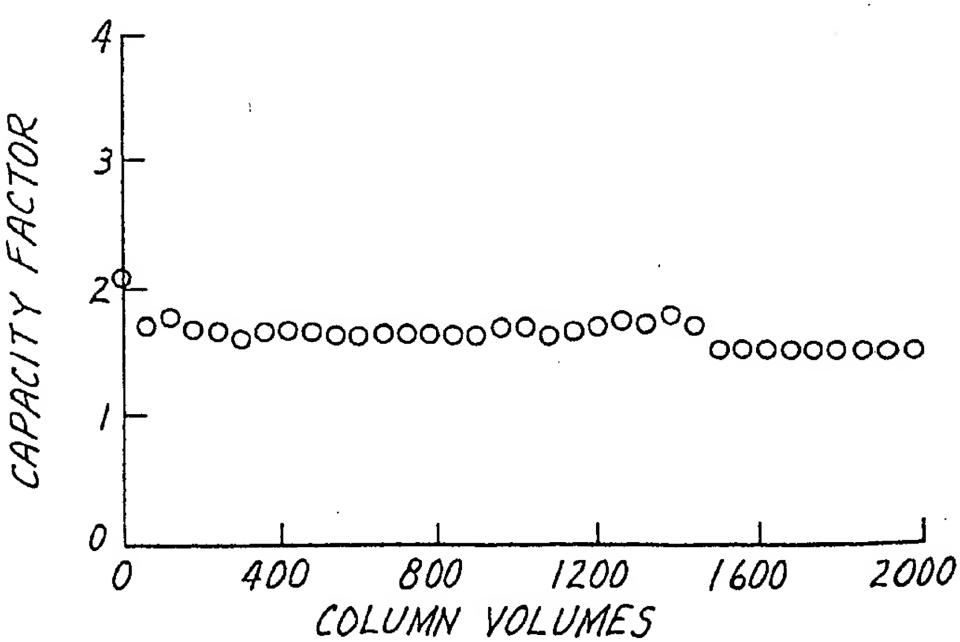

4
3
2
1
0
CAPACITY FACTOR
0
400
800
1200
1600
2000
COLUMN VOLUMES

FIG. 10

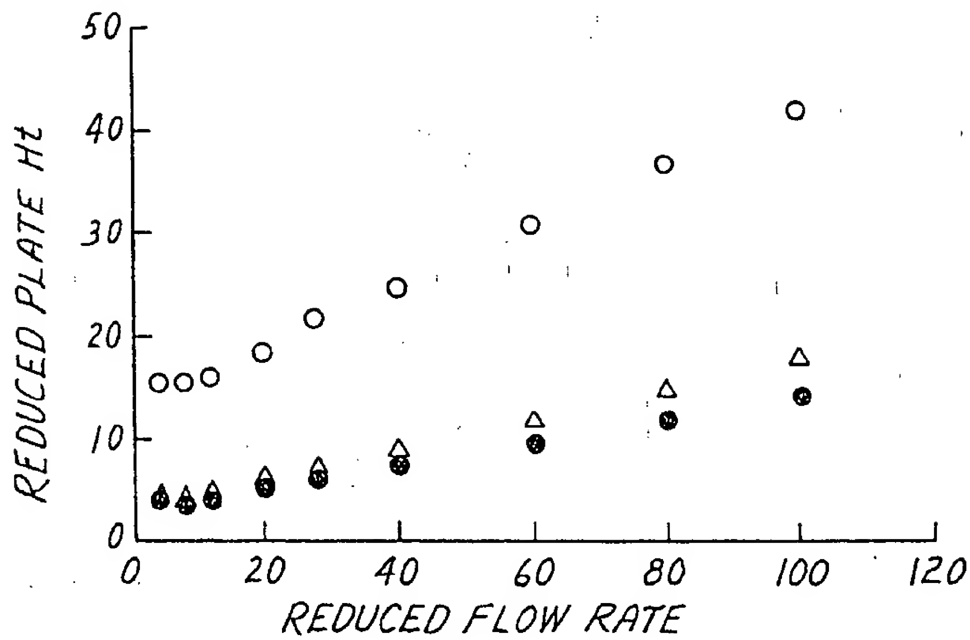

50
40
30
20
10
0
REDUCED PLATE Ht
0
20
40
60
80
100
120
REDUCED FLOW RATE

FIG. 8A

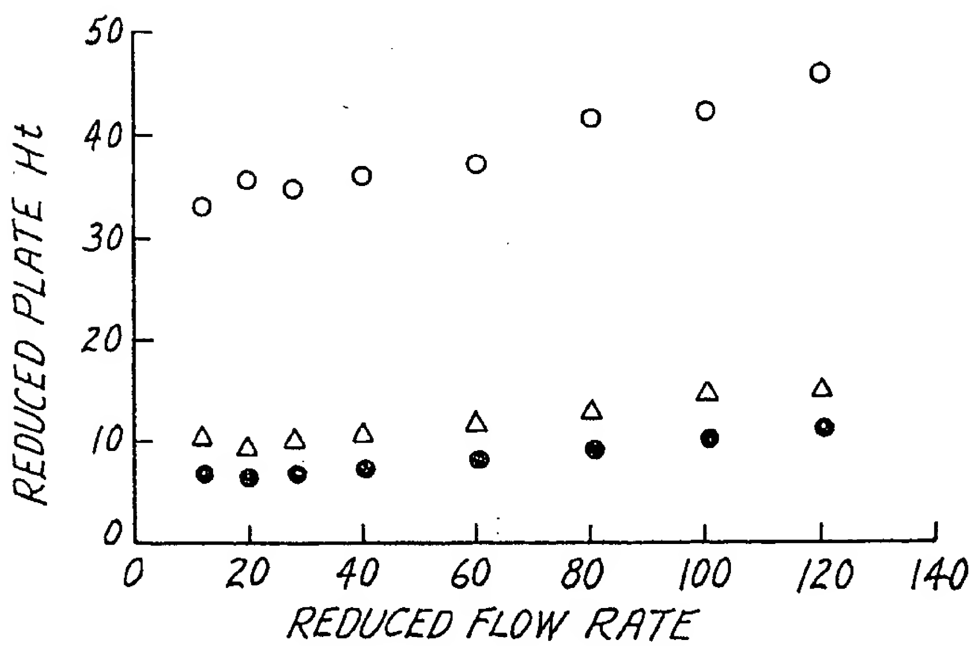
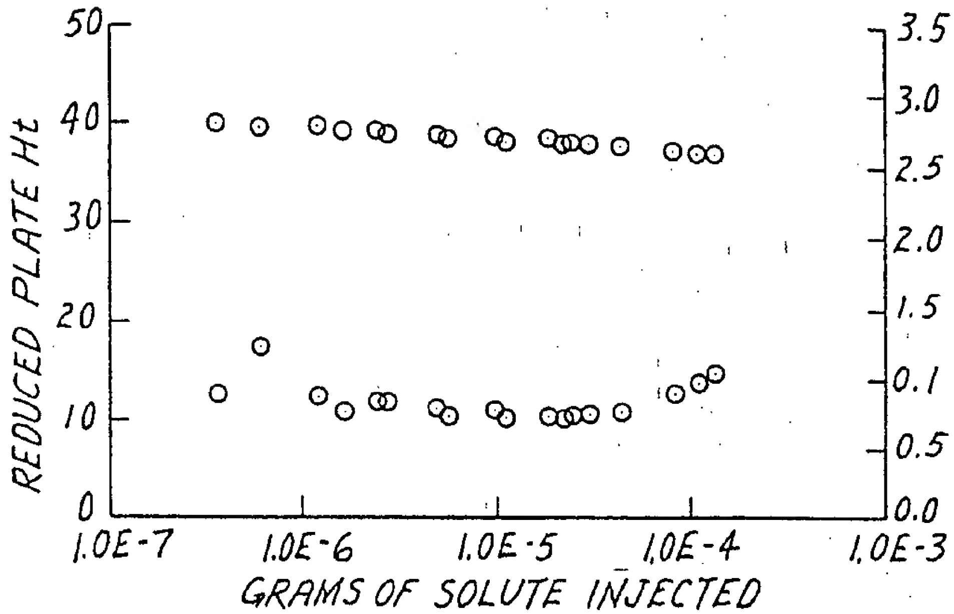
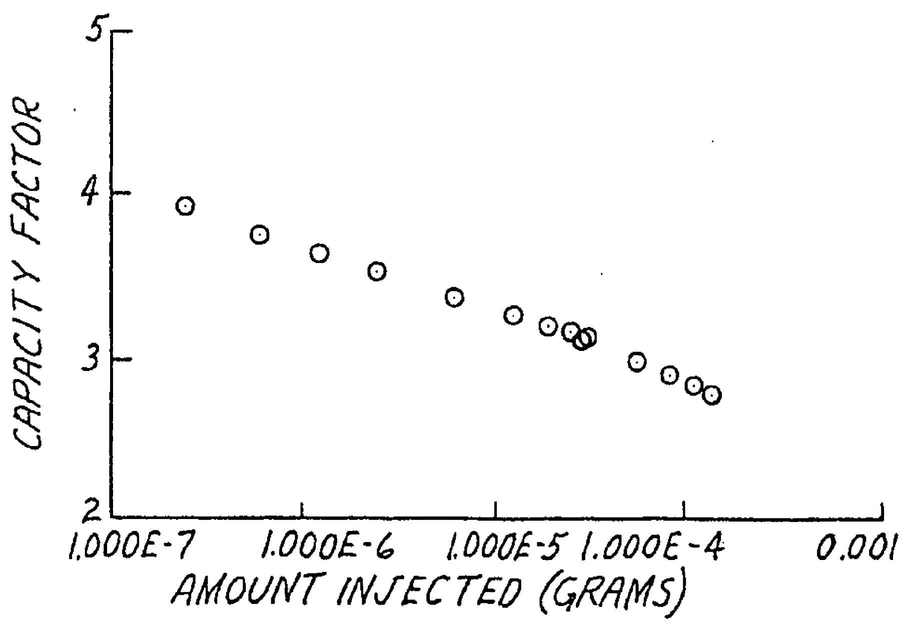

50
40
30
20
10
0
REDUCED PLATE Ht
0
20
40
60
80
100
120
140
REDUCED FLOW RATE

FIG. 8B



50
40
30
20
10
0
REDUCED PLATE Ht
3.5
3.0
2.5
2.0
1.5
0.1
0.5
0.0
1.0E-7
1.0E-6
1.0E-5
1.0E-4
1.0E-3
GRAMS OF SOLUTE INJECTED

FIG. 9A



5
4
3
2
CAPACITY FACTOR
1.000E-7
1.000E-6
1.000E-5
1.000E-4
0.001
AMOUNT INJECTED (GRAMS)

FIG. 9B

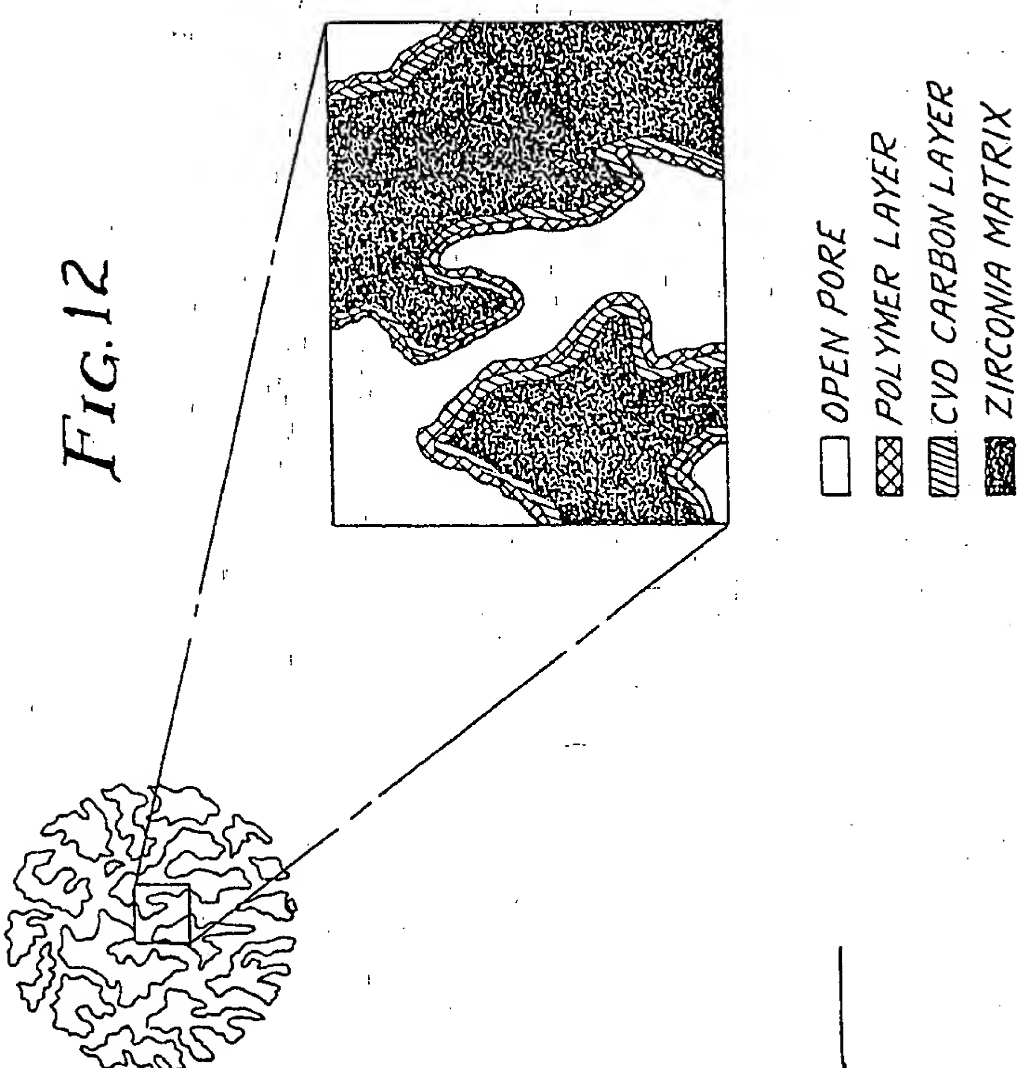

OPEN PORE
POLYMER LAYER
CVD CARBON LAYER
ZIRCONIA MATRIX

FIG. 12

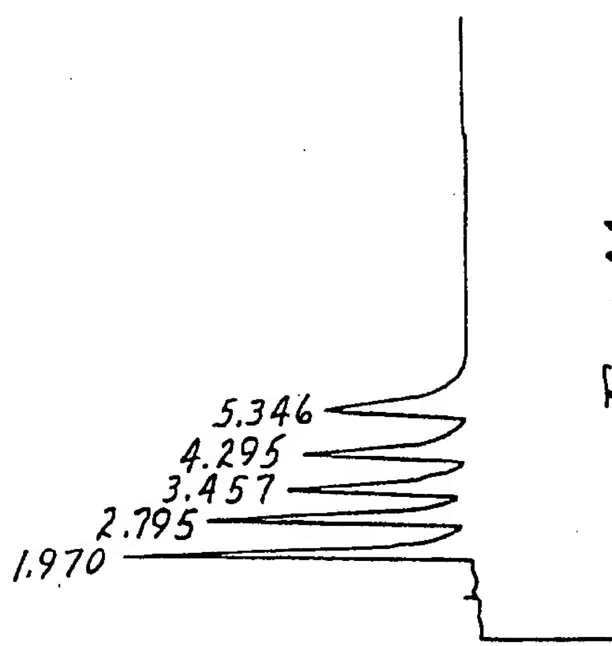

5.346
4.295
3.457
2.795
1.970

FIG. 11

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(54) Carbon-clad inorganic oxide particles with a polymer coating thereon.

(57) A carbon-clad inorganic oxide particle having an outermost cross-linked polymer coating. Carbon-clad inorganic oxide particles may be formed by placing a plurality of the particles in a reaction chamber, elevating the temperature within the chamber, reducing the pressure within the chamber, and introducing into the chamber a vapor comprising carbon and thermally decomposing the vapor so as to deposit a cladding of carbon onto the particles. The carbon-clad particles may be coated with a monomer or an oligomer followed by cross-linking the monomer or oligomer to provide polymer-coated carbon-clad inorganic oxide particles.

EP 0 635 301 A3

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 11 3956

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
A	FR-A-2 522 282 (CAN MED) * page 1, line 27 - page 2, line 35 * * page 3-4; example 1 * ---	1,2,4,12	B01J20/32 B01J20/02 G01N30/48
A	EP-A-0 331 283 (REGENTS OF THE UNIV. OF MINNESOTA) * page 5, line 20 - page 7, line 33 * ---	1-5,10,11	
A	US-A-3 901 808 (BOKROS) * column 2, line 30 - column 3, line 41 * ---	7-9	
A	US-A-3 822 530 (FULLER) * column 1, line 56 - column 3, line 26 * ---	1-5	
A	US-A-3 565 762 (H.NICKEL) * column 4, line 38-55 * ---	1,4	
A	US-A-4 349 462 (L. VELENYI) * column 4, line 32-51 * -----	1,4	

TECHNICAL FIELDS SEARCHED (Int.Cl.5)

B01J
G01N

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	25 January 1995	Wendling, J-P

CATEGORY OF CITED DOCUMENTS

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